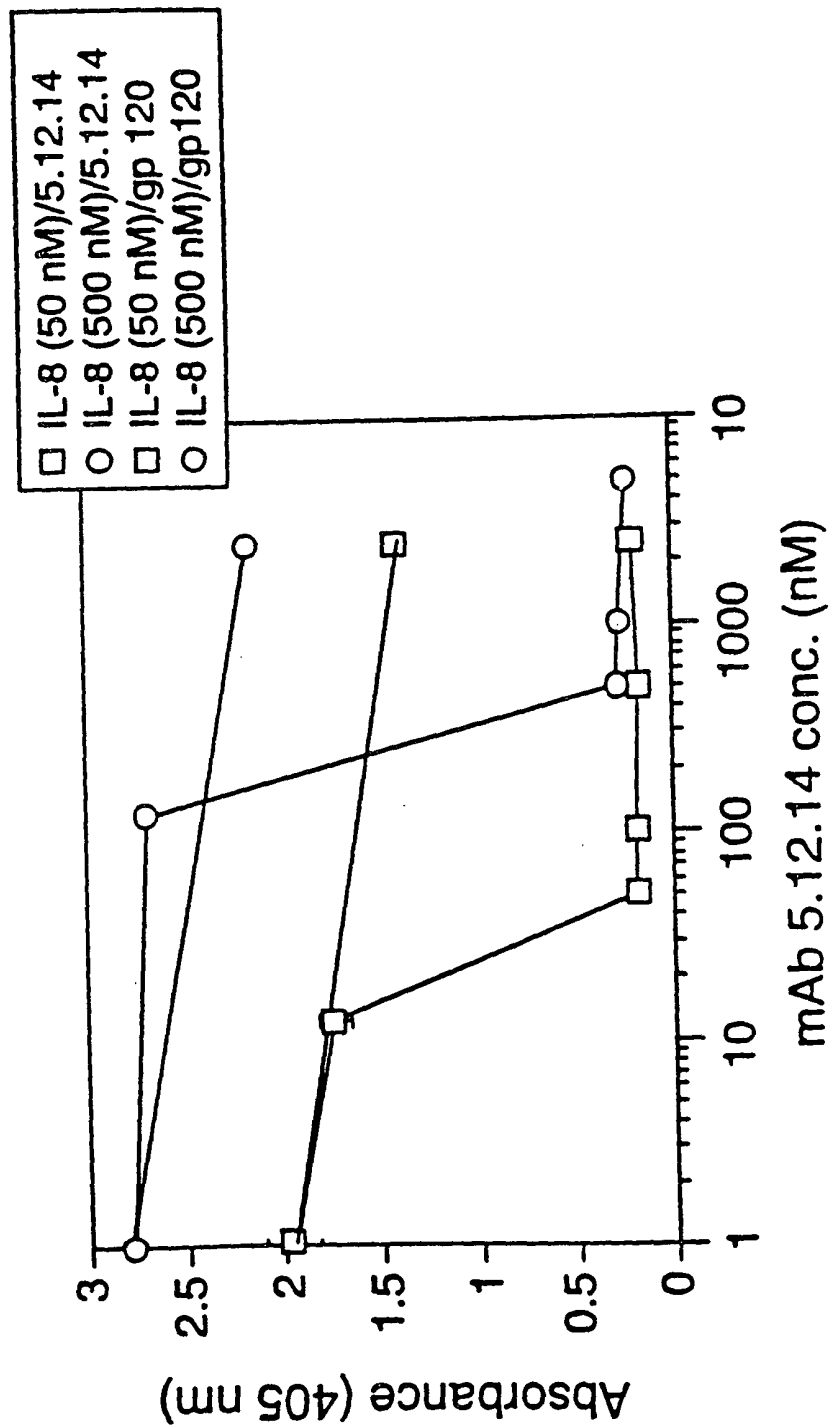
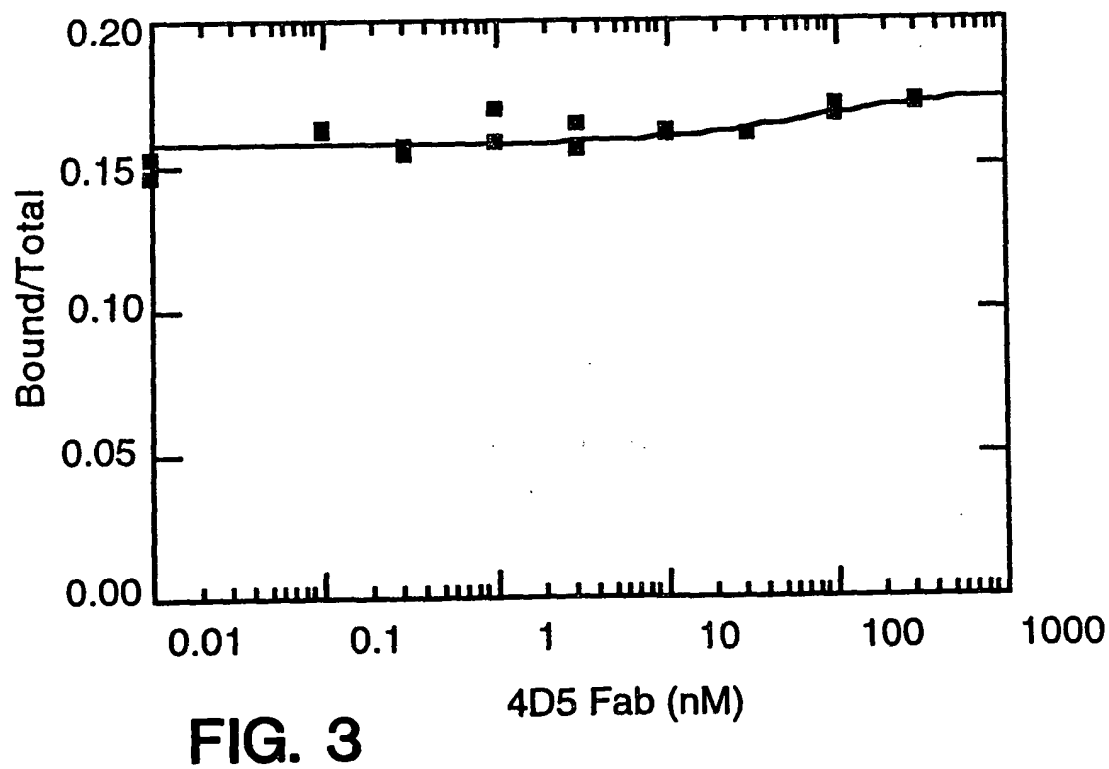
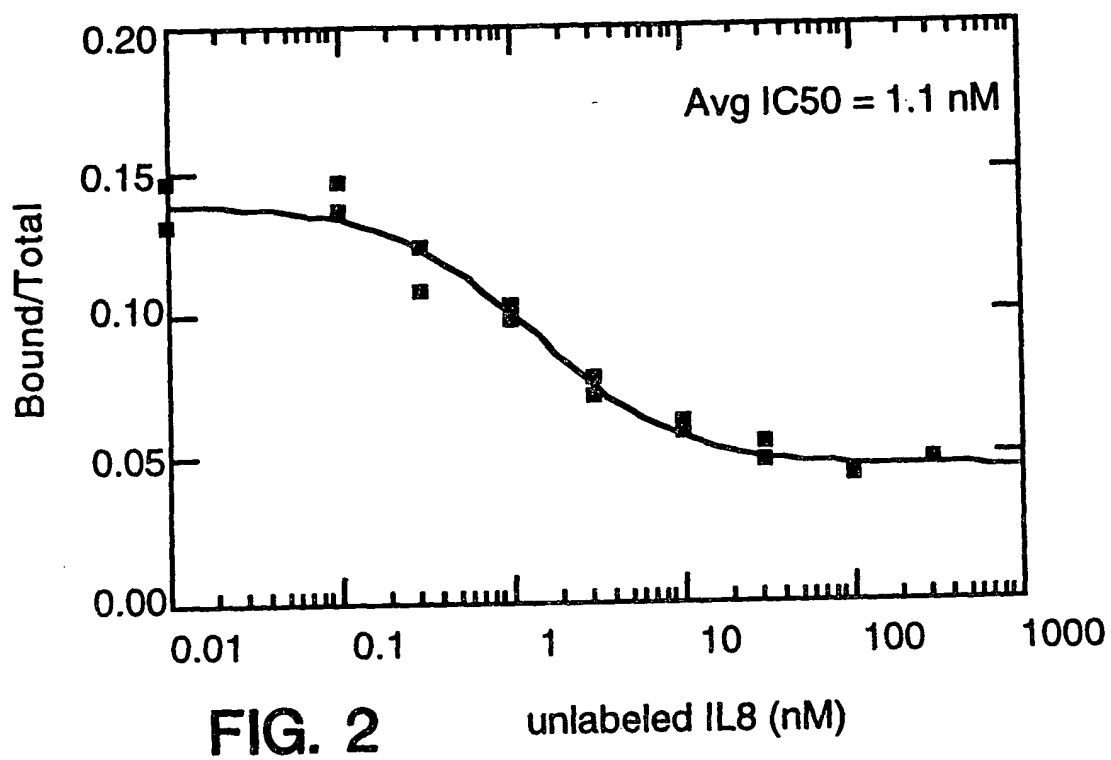
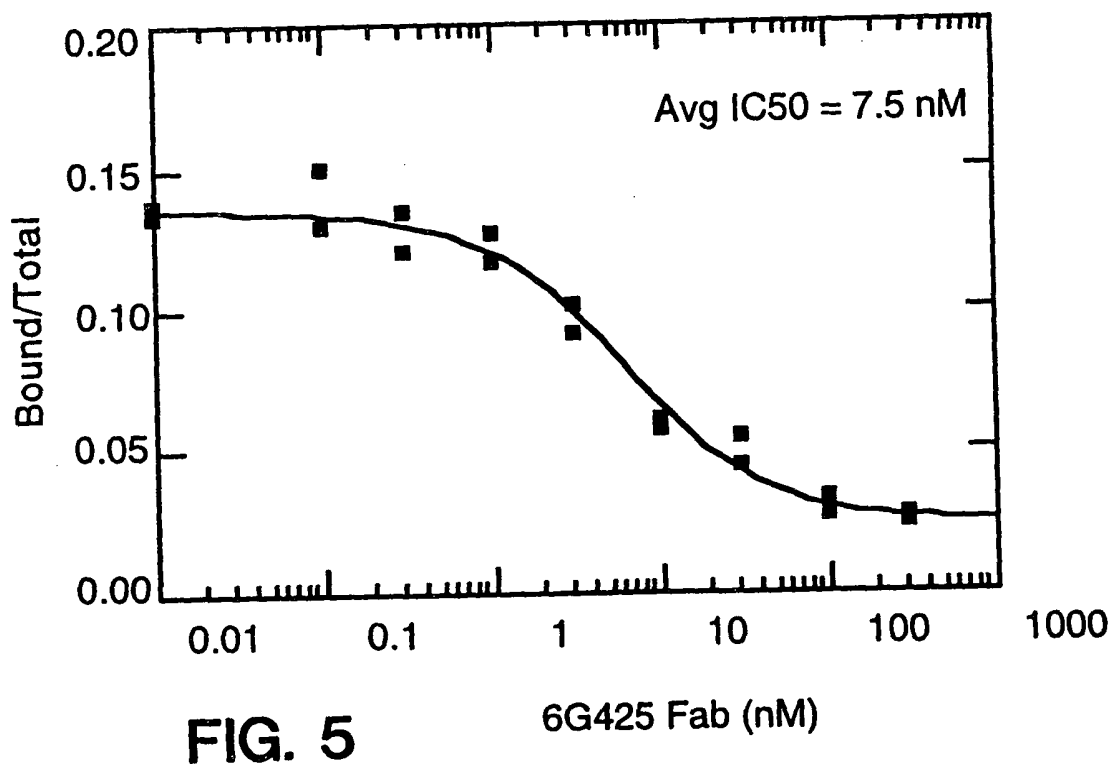
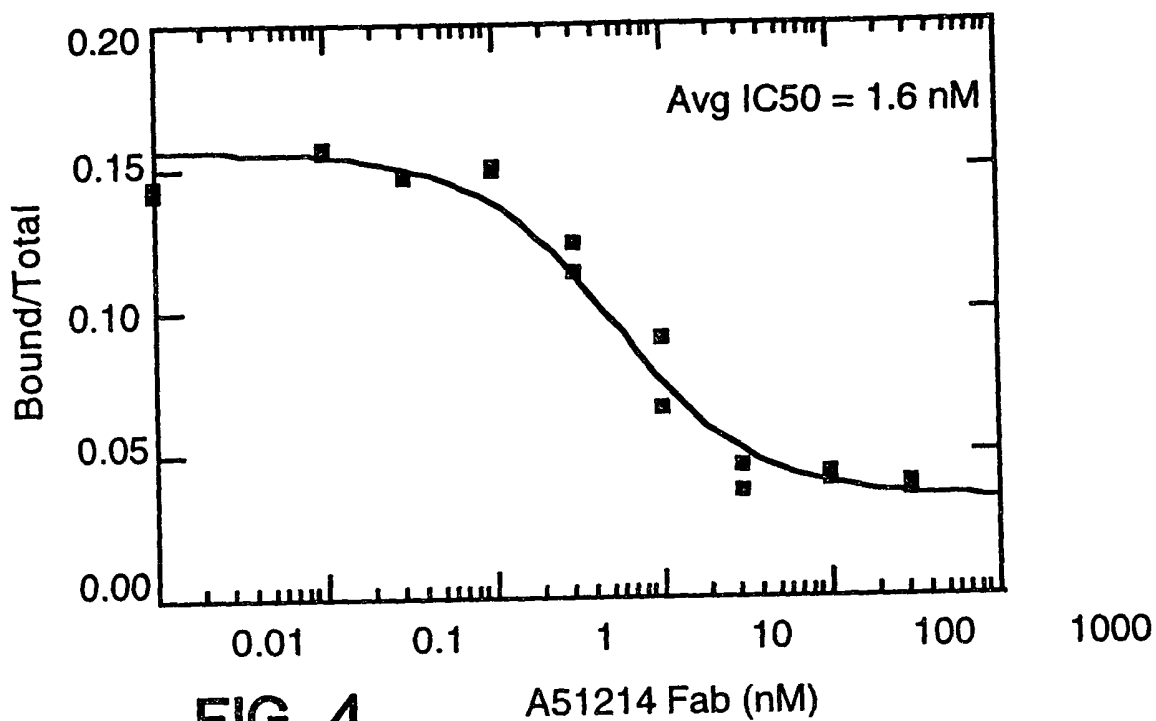


FIG. 1







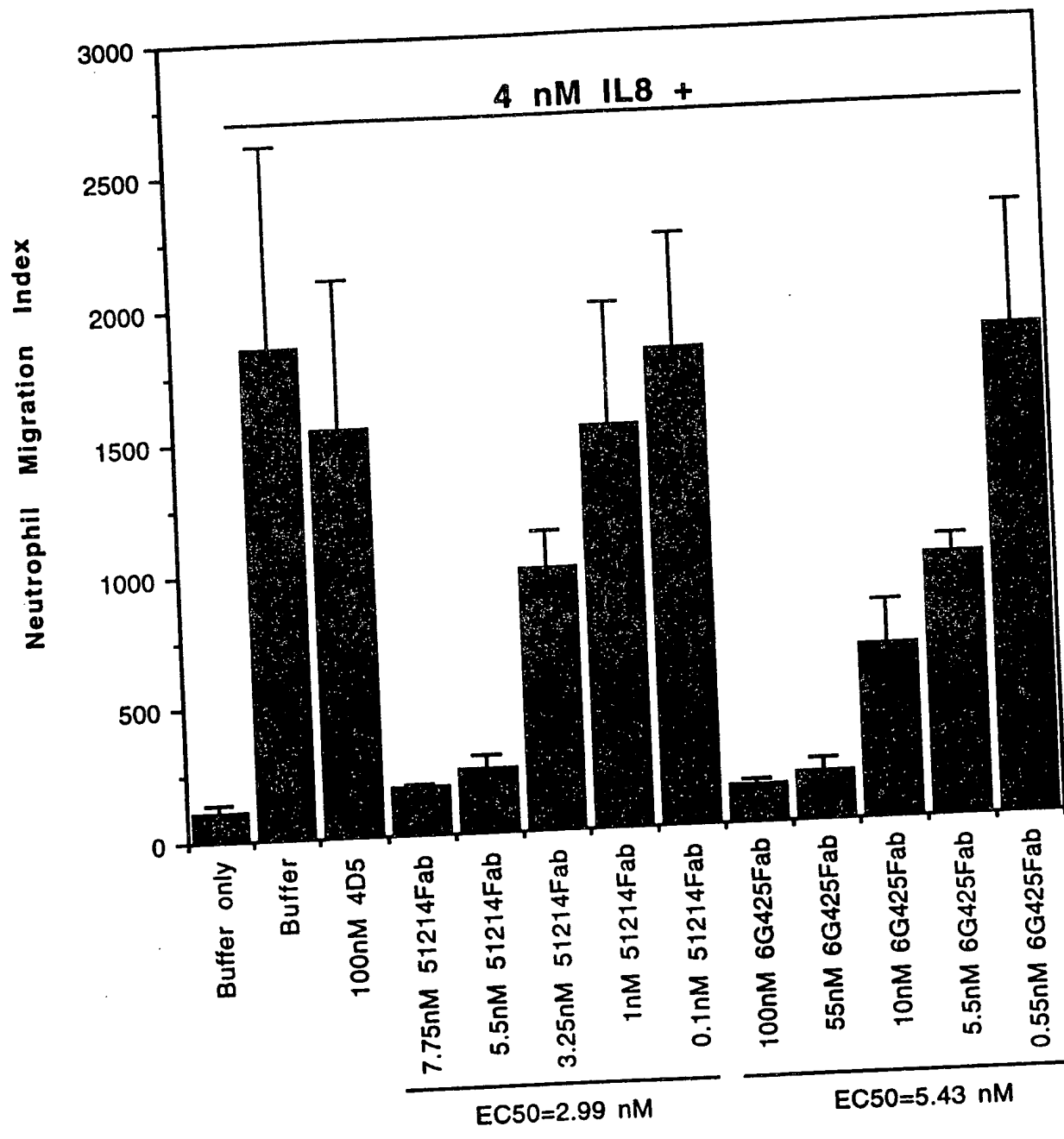


FIG. 6

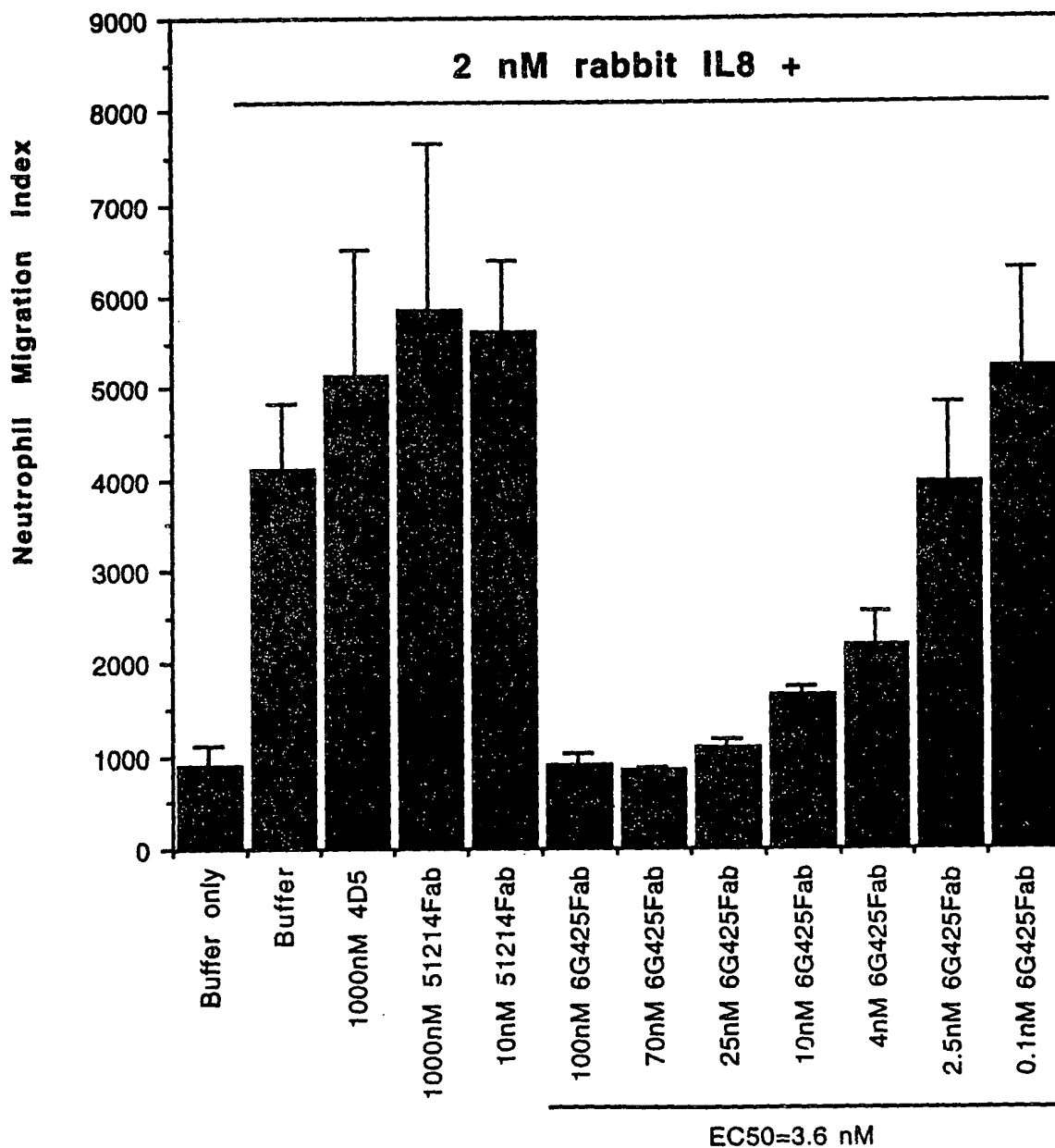


FIG. 7

FIG. 8

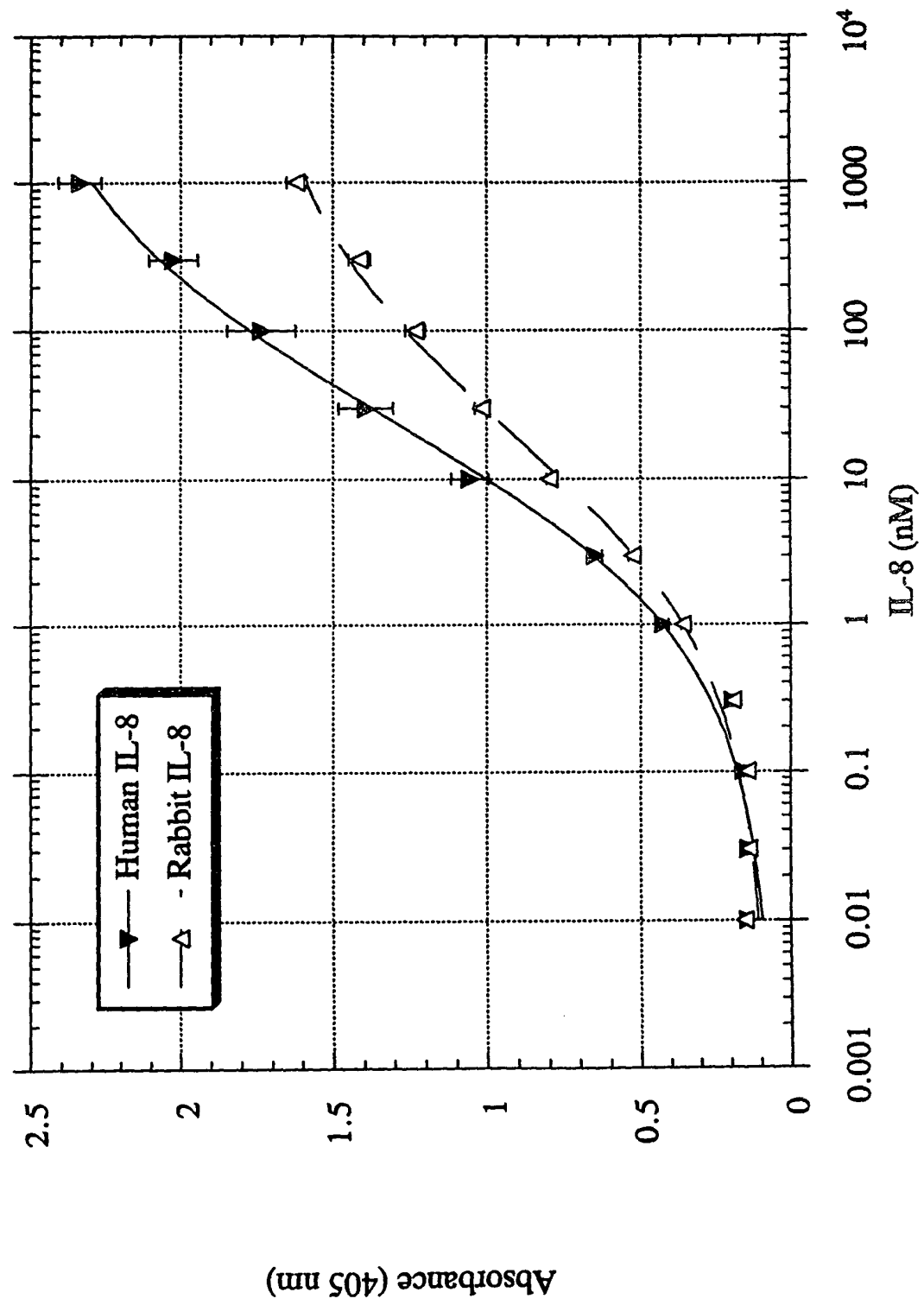


FIG. 9

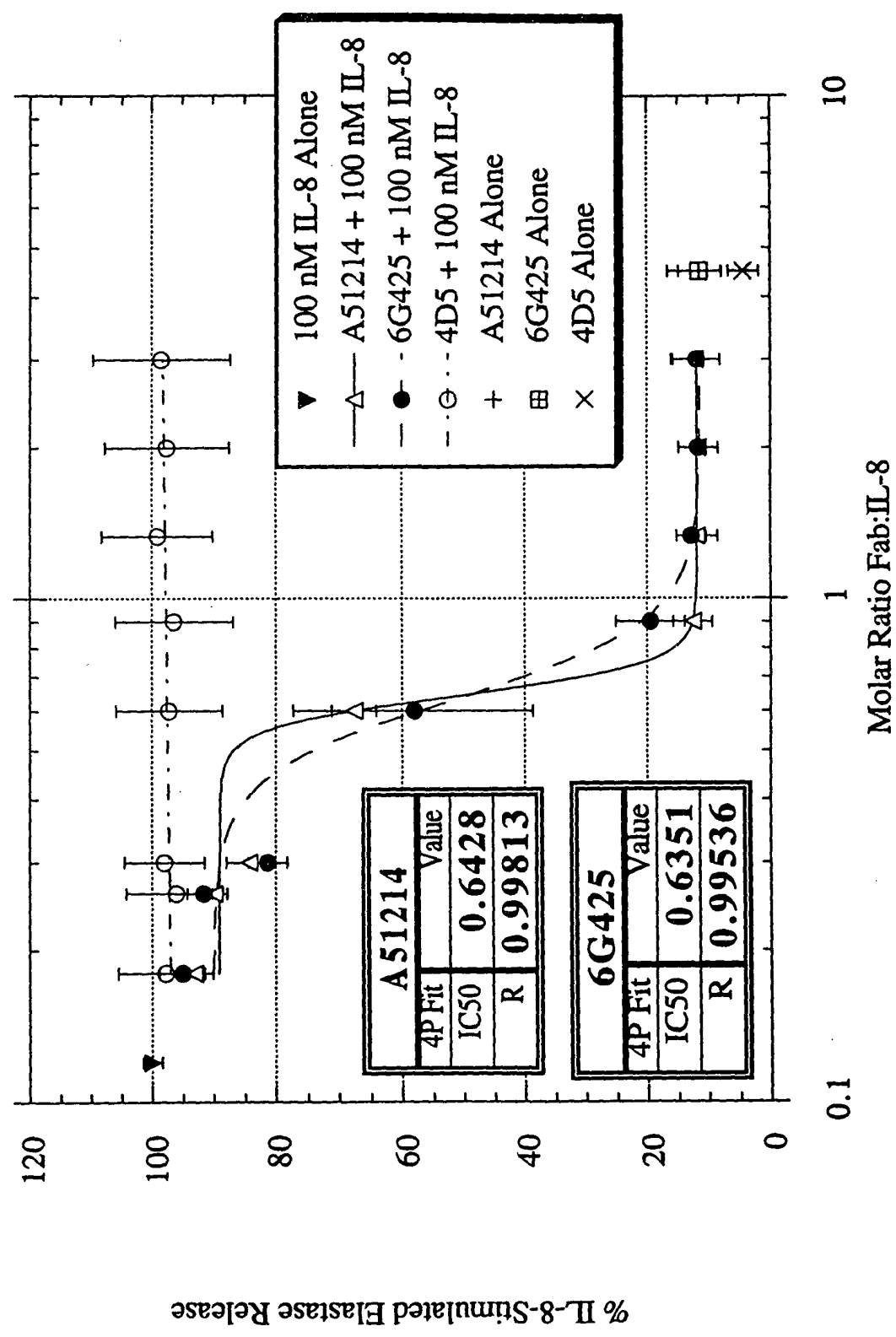
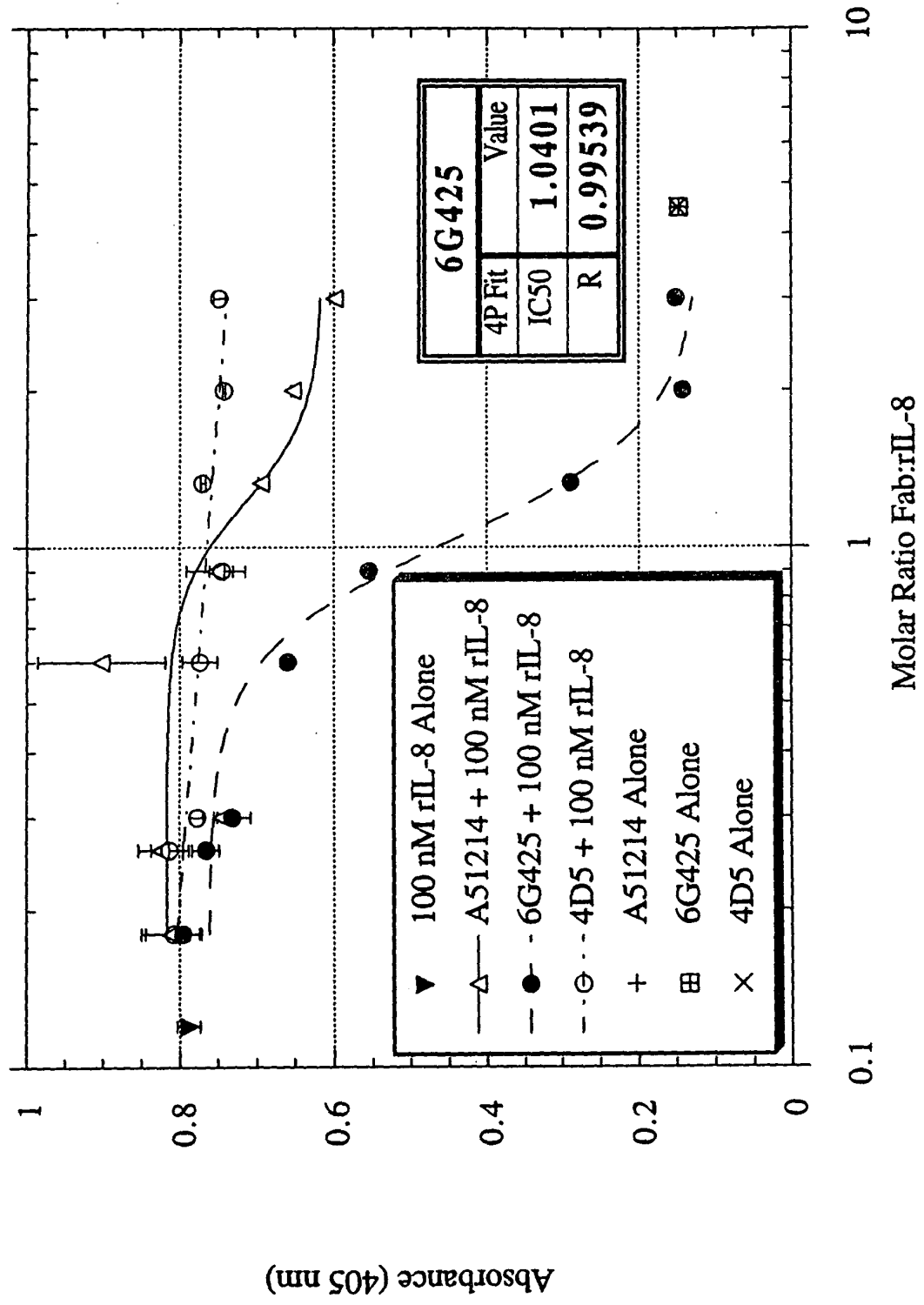


FIG. 10



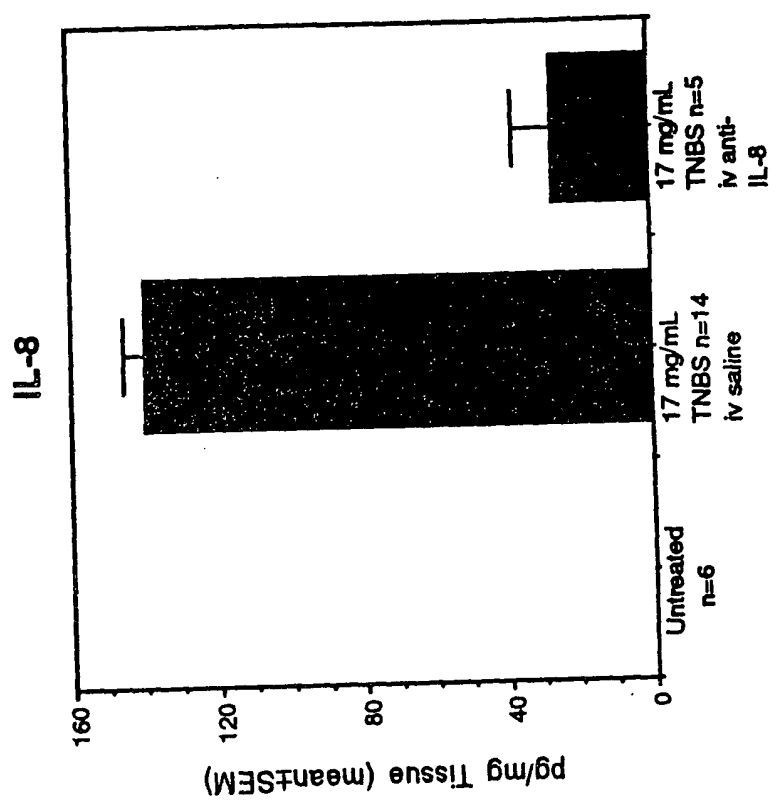


FIG. 11B

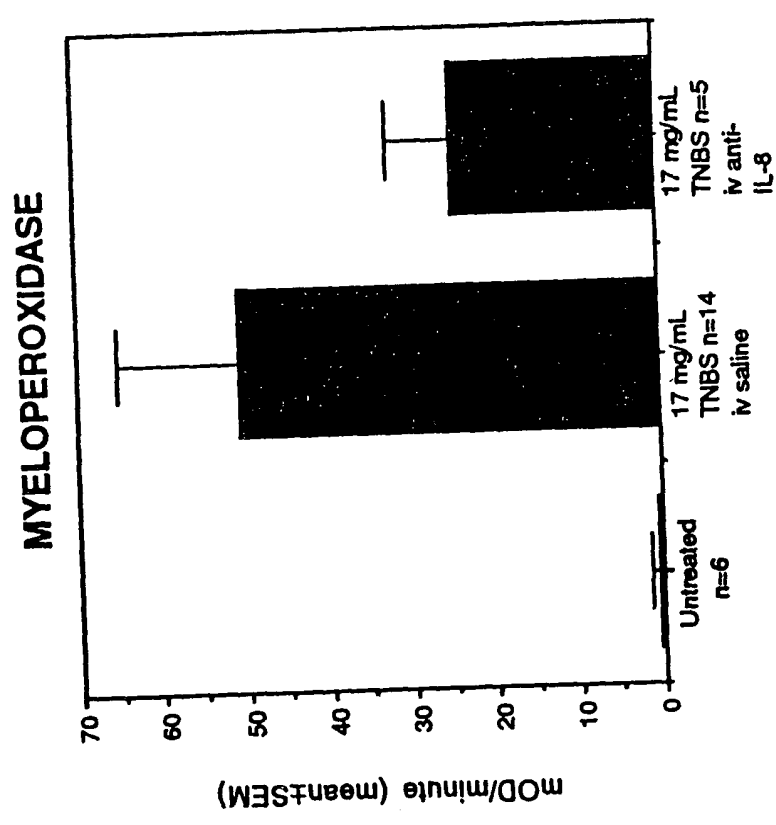


FIG. 11A

TOP SECRET

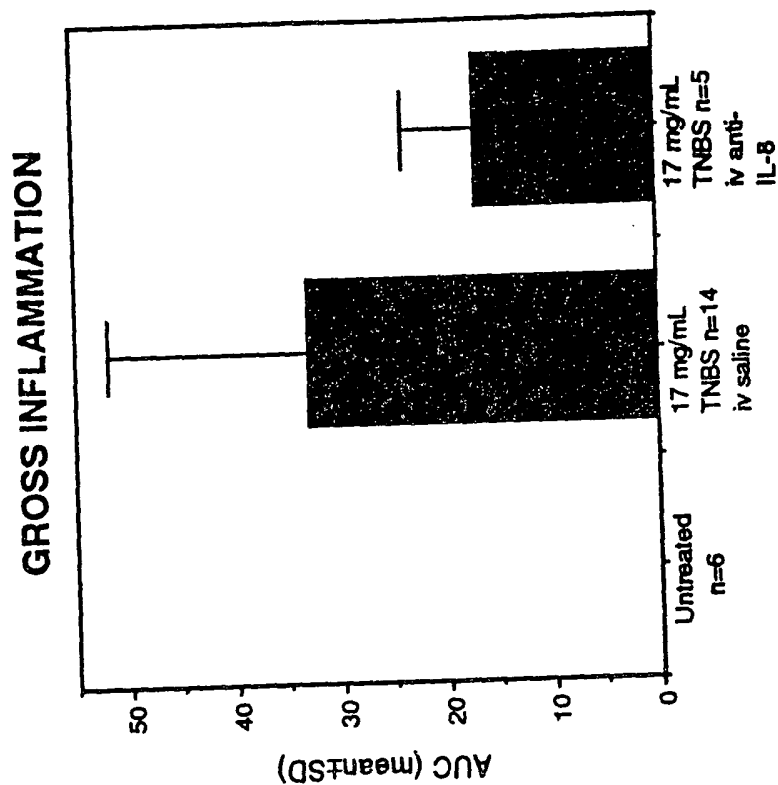


FIG. 11D

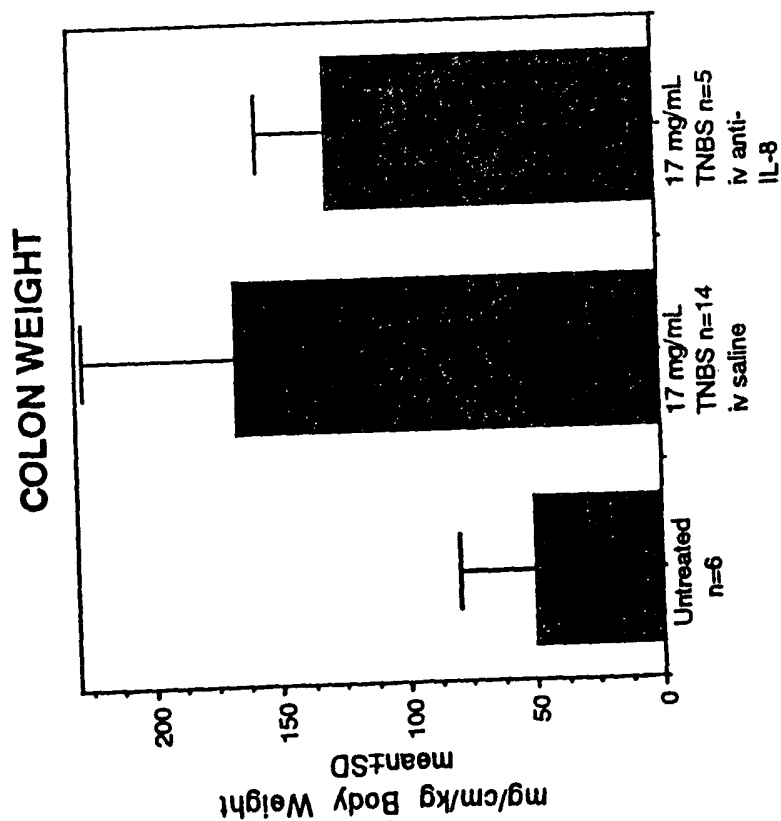


FIG. 11C

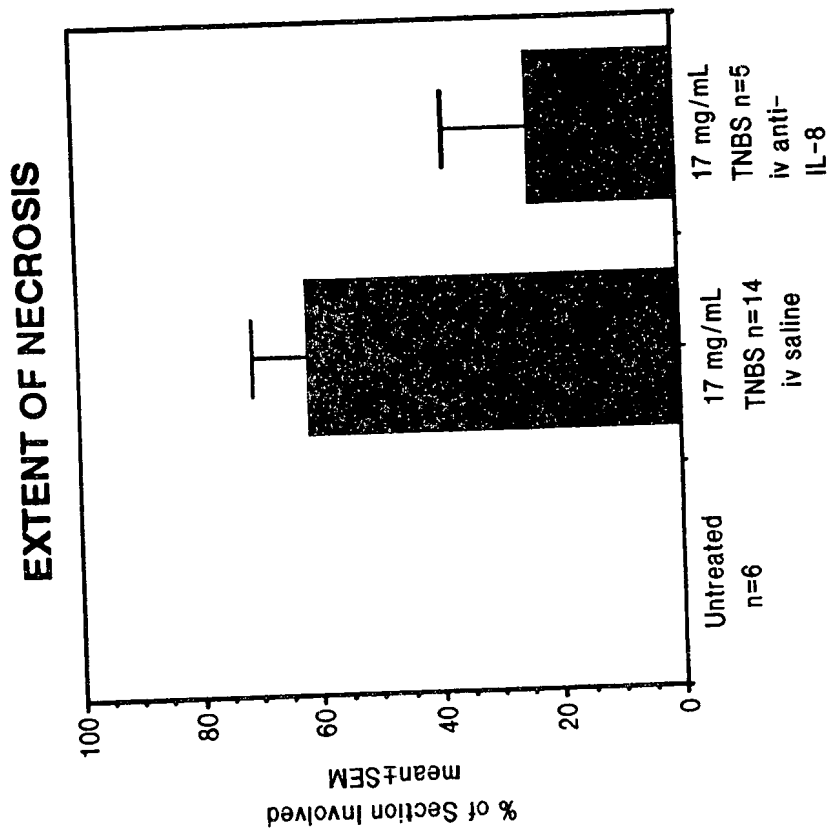


FIG. 11F

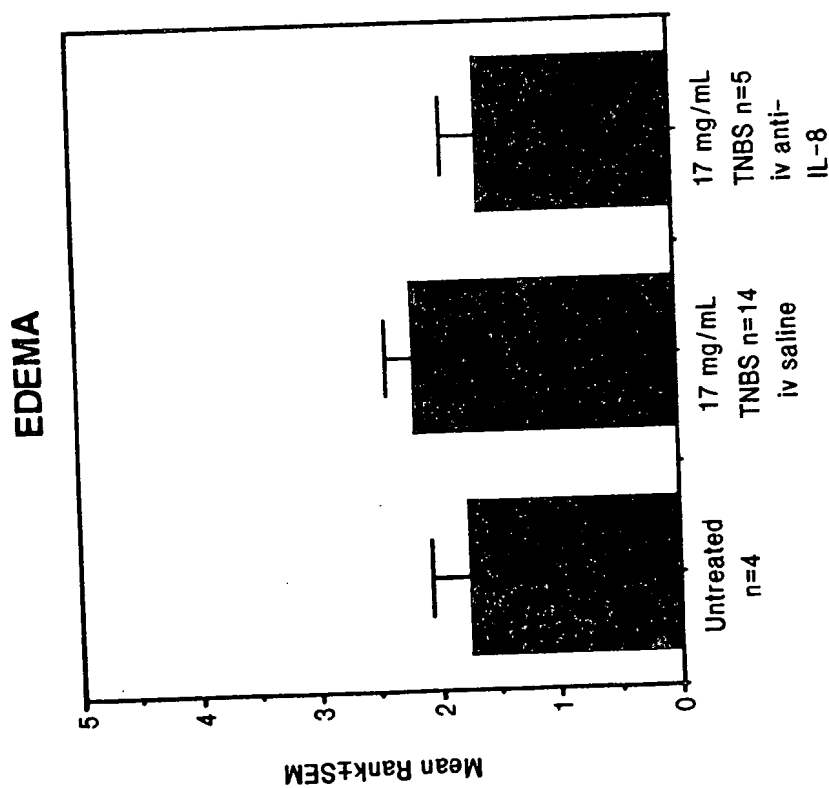


FIG. 11E

10750-00002-00

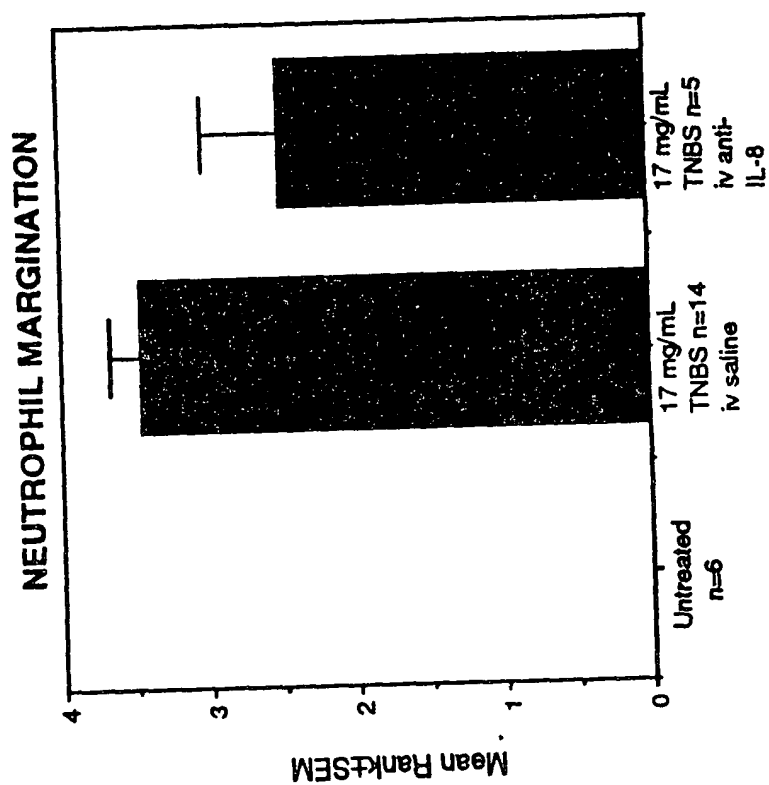


FIG. 11H

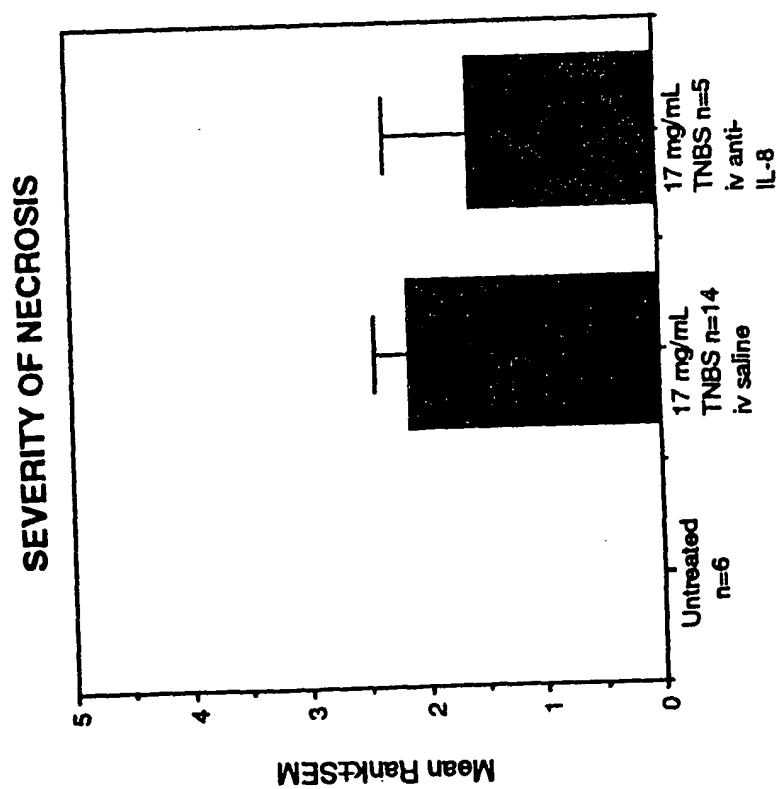


FIG. 11G

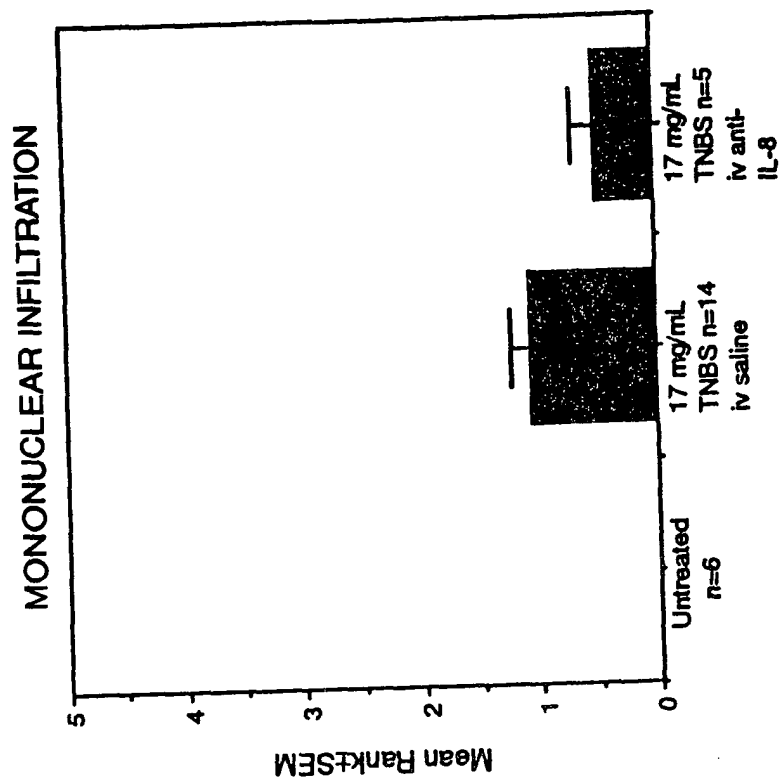


FIG. 11J

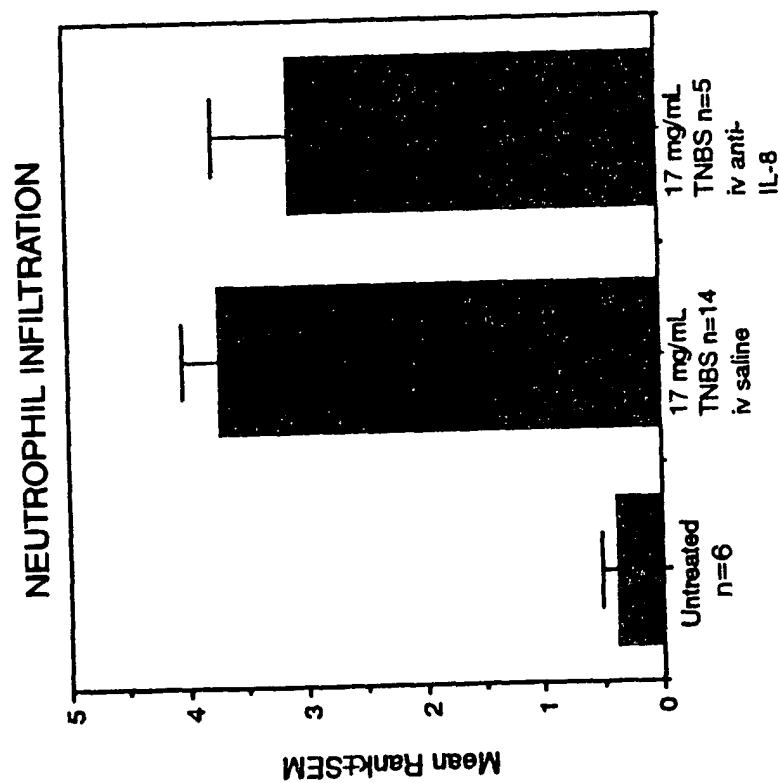
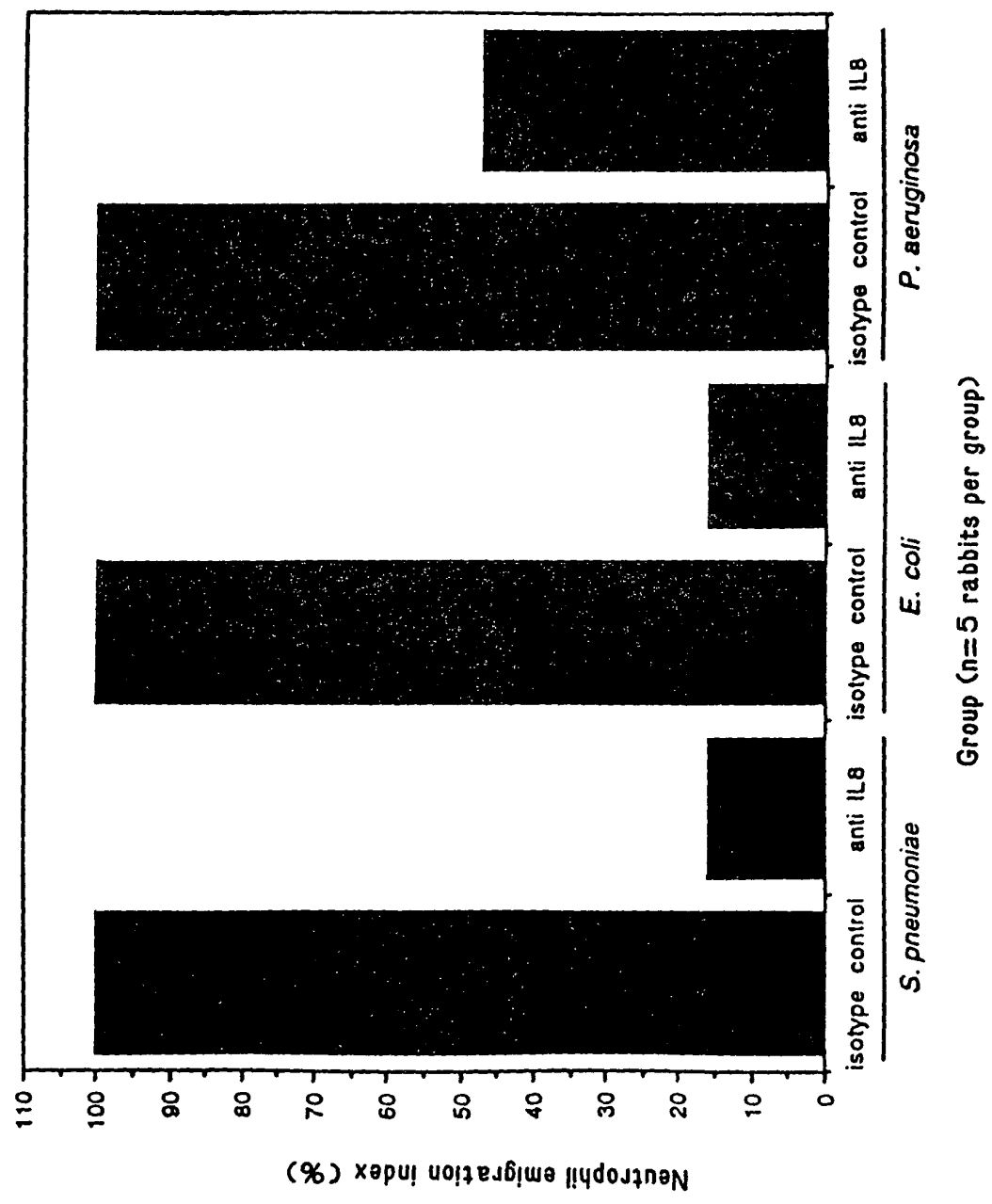


FIG. 11I

FIG. 12



Light Chain Primers:

FIG. 13

MKLC-1, 22mer

5' CAGTCCAACTGTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

695555-0001

FIG. 14

Light chain forward primer

SL001A-2 35 mer

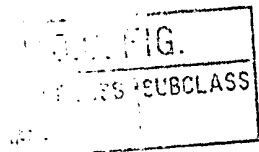
5' ACAACGCGTACGCT GACATCGTCATGACCCAGTC 3' (SEQ ID NO.7)
T T (SEQ ID NO.8)
A (SEQ ID NO.9)

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3' (SEQ ID NO.10)

TOP SECRET



Heavy chain forward primer

SL002B 39 mer

5' CGATGGCCCCG ATAGACCGATGGGCGTGTGTTTGGC 3' (SEQ ID NO.11)
C
T (SEQ ID NO.12)
G (SEQ ID NO.13)
A (SEQ ID NO.14)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGCCCCG ATAGACCGATGGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
T (SEQ ID NO.15)
A (SEQ ID NO.14)
G (SEQ ID NO.13)

1 GACATTGTCA TGACACAGTC TCATAAATTC ATGTCCACAT CAGTAGGAGA CAGGTCAGC
CTGTAACAGT ACTGTGTCAG AGTTTTTAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGCTTTTGGT
21 V T C K A S O N V G T N V A W Y Q Q K P

* * * * *
CDR #1

121 GGGCAATCTC CTAAGCACT GATTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT
CCCGTTAGAG GATTTCGTGA CTAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA
41 G Q S P K A L I Y S S Y R Y S G V P D

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT
GGAAAGTGTC CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGATGTCGGT ACACGTCAGA
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATT CTGTACAGCA TATAACATCT ATCCTCTCAC GTTCGGTCTT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA
81 E D L A D Y F C Q Q Y N I Y P L T F G P

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGCTGAT GCTGCACCAC CAACTGTATC CATCTTCCCA
CCCTGGTTCG ACCTCAACTT TGCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGGT
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCATTTCGAA (SEQ ID NO.16)

GGTAAGCTT (SEQ ID NO.17)

121 P F E

FIG. 16

1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
AAGATAACGA TGTTTGCGCA TGCGACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA
1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCATAT TCAGTAGTTA
CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT
13 P P G G S L K L S C A A S G F I F S S Y
* *

CDR #1

121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCG CAACCATTAA
ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCAGC GTTGGTAATT
33 G M S W V R Q T P G K S L E L V A T I N
* * * * *

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG
ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAGT GGTAGAGGGC
53 N N G D S T Y Y P D S V K G R F T I S R
* * * * *

CDR #2

241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
TCTGTTACCG TTCTTGTTGGG ACATGGACGT TTA CTCTGCA GACTTCAGAC TCCTGTGTCTG
73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA
GTACAAAATG ACACGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGGT
93 M F Y C A R A L I S S A T W F G Y W G Q
* * * * *

CDR #3

361 AGGGACTCTG GTCAGTGTCT CTGCAGCCAA AACAACAGCC CCATCTGTCT
TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCTG GGTAGACAGA
113 G T L V T V S A A K T T A P S V Y

ApaI

411 ATCCGGG (SEQ ID NO.18)
TAGGCCC (SEQ ID NO.19)
130 P

FIG. 17

FIG. 18

VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3' (SEQ ID NO.20)

VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3' (SEQ ID NO.21)

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3' (SEQ ID NO.22)

VH.rear 33-MER

5' GATGGGCCCTTG GTGGAGGCTGCAGAGACAGTG 3' (SEQ ID NO.23)

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC
CGCATGCGAC TATAGCAGTA CTGTGTGAGA GTTTTAAAGT ACAGGTGTAG TCATCCTCTG
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
TCCAGTCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
18 R V S V T C K A S O N V G T N V A W Y Q
* * * * *

CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA
GTCTTTGGTC CCGTTAGAGG ATTTCTGTGAC TAAATGAGCA GTAGGATGGC CATGTCACCT
38 Q K P G Q S P K A L I Y S S S Y R Y S G
* * * * *

CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTGAGCAAT ATAACATCTA TCCTCTCACG
CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
78 V Q S E D L A D Y F C Q Q Y N I Y P L T
* * * * *

CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
AAGCCAGGAC CCTGGTTCGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTGGCT CTGTTGTGTG CCTGCTGAAT
AAGGGCGGTA GACTACTCGT CAACCTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTAGCCCA
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
TTGAGGGTCC TCTCACAGTG TCTCGTCCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTG
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC
TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
GTAGTCCCGG ACTCGAGCGG GCAGTGTTC TCGAAGTTGT CCCCTCTCAC
198 H Q G L S S P V T K S F N R G E C (SEQ ID NO.25)

711 TTAA (SEQ ID NO.24)
AATT
216 O

FIG. 19

09726238-033101

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
CGCATGCGAC TCCACGTCTGA CCACCTCAGA CCCCCTCCGA ATCACGGCGG ACCTCCCAGG
-3 A Y A E V Q L V E S G G G L V P P G G S

121 CTGAAACTCT CCTGTGCAGC CTCTGGATTC ATATTCAGTA GTTATGGCAT GTCTTGGGTT
GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA
18 L K L S C A A S G F I F S S Y G M S W V
* * * *

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
GCGGTCTGAG GTCCGTTCTC GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
38 R Q T P G K S L E L V A T I N N N G D S
* * * * *

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
TGGATAATAG GTCTGTCACA CTTCCCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
58 T Y Y P D S V K G R F T I S R D N A K N
* * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTAAGTGTGCA
TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT
78 T L Y L Q M S S L K S E D T A M F Y C A

361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTTACTGGG GCCAAGGGAC TCTGGTCACT
TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAGTGA
98 R A L I S S A T W F G Y W G Q G T L V T
* * * * *

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
118 V S A A S T K G P S V F P L A P S S K S

481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
TGGAGACCCC CGTGTCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC
138 T S G G T A A L G C L V K D Y F P E P V

541 ACGGTGTCGT GGAAGTCAAG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCTTA
TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
158 T V S W N S G A L T S G V H T F P A V L

601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG
178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A

661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
 TGGGTCTGGA TGAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
 198 T Q T Y I C N V N H K P S N T K V D K K
 721 GTGAGCCCA AATCTTGTGA CAAACTCAC ACATGA (SEQ ID NO.26)
 CAACTCGGT TTAGAACACT GTTTGAGTG TGTACT
 218 V E P K S C D K T H T O (SEQ ID NO.27)

FIG. 20B

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAAC TGTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 21

Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3' (SEQ ID NO.28)
 T T T A A
 (SEQ ID NO.29)
 (SEQ ID NO.30)

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3' (SEQ ID NO.31)

FIG. 22

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3' (SEQ ID NO.32)
T C (SEQ ID NO.33)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
T A G (SEQ ID NO.15)
(SEQ ID NO.14)
(SEQ ID NO.13)

FIG. 23

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTCACA
TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * *

301 CTCAGGATCA GCAGAGTGGG GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * *

CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCC ACTACGACGT
98 H V P L T F G A G T K L E L K R A D A A
* * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA (SEQ ID NO.34)
GGTTGACATA GGTAAGGG TGGTAGGTCA CTCGTTAACT
118 P T V S I F P P S S E Q L K (SEQ ID NO.35)

FIG. 24

70 G AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * * *

CDR #1

181 AAGCAGAGCC ATGGAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTGC
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

BstEII ApaI
421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGCC
CAGTGGCAGA GGAGGCGGAT TTGGCTGTCG GGGTAGCCAG ATAGGCCCGG
118 V T V S S A K T D S P I G L S G P

471 CATC (SEQ ID NO.36)
GTAG
135 I (SEQ ID NO.37)

FIG. 25

FIG.

SUBCLASS

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3' (SEQ ID NO.39)

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SEQ ID NO.40)

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

FIG. 26

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAT
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATAACAAGC AAAAAAGATA ACGATGTTTA
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
CGTATGCGAC TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
-3 A Y A D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAAG ATCTAGTCAG AGCCTTGTCAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTCACA
TTGGCTAAAA GACCCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * * *

CDR #3

361 CATGTTCCGC TCACGTTCCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCTGG TTCGACCTCG ACTTTGCCCG ACAACGACGT
98 H V P L T F G A G T K L E L K R A V A A
* * * * *

421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT
GGTTGACATA AGTAGAAGGG TGGTAGGTCA CTCGTTAACT TTAGACCTTG ACGGAGACAA
118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCTGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A

SECRET

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGCGAGT GTTCTCTCGAA GTTGTCCTCCCT
 198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTAA (SEQ ID NO.41)
 CTCACAATT
 218 E C O (SEQ ID NO.42)

FIG. 27B

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
-3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCTC GGAATCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCCTTC CGGTGTAAGT GACATCTGTG TAGAAGGTGC
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

421 GTCACCGTCT CCTCCGCCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG
118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA
TTCTCGTGGA GACCCCCGTG TCGCCGGGAC CCGACGGACC AGTTCCTGAT GAAGGGGCTT
138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG GCGTGCACAC CTTCCC GGCT
GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTCGC CGCACGTGTG GAAGGGCCGA
158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTA CTCTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC
CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCGTGC
178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A

FIG. 28B

661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTCGTTGTG GTTCCACCTG
198 L G T Q T Y I C N V N H K P S N T K V D
721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA (SEQ ID NO.43)
TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT
218 K K V E P K S C D K T H T O (SEQ ID NO.44)

FIG. 28B

69663-03104

Variable Light Chain Domain

```

      10      20      abcde 30      40
6G425  DIVMTQTPLSLPVS LGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
F(ab)-1 DIQMTQSPSSLSASV GDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
humkI  DIQMTQSPSSLSASV GDRVTITCRASKTI----SKYLAWYQQKPGKAPKLLIY
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
      =====
      ++++++++
      L1

      50      60      70      80      90      100
6G425  YKVS NRFS GVPDR FSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR (SEQ ID NO.45)
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
F(ab)-1 YKVS NRFS GVPDR FSDSGSGTDFTLTISSLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR (SEQ ID NO.46)
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
humkI  YSGSTLES GVPDR FSDSGSGTDFTLTISSLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR (SEQ ID NO.47)
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
      ===
      ++++++++
      L2
      ++++++++
      L3
```

Variable Heavy Chain Domain

```

      10      20      30      40
6G425  EIQLQQSGPELMKPGASVKISCKASGYFSSSHYMHVWKQSHGKSLEWI
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
F(ab)-1 EVQLVESGGGLVQPGGSLRLSCAASGYFSSSHYMHVWRQAPGKGLEWV
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
humIII EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNWRQAPGKGLEWV
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
      =====
      +++++
      H1

      50 a      70      80 abc      90      100      110
6G425  GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT (SEQ ID NO.48)
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
F(ab)-1 GYIDPSNGETTYNQKFKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT (SEQ ID NO.49)
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
humIII  GMIHPSDSETRYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGIYFY-GTTYFDYWQGT (SEQ ID NO.50)
      # # # # # # # # # # # # # # # # # # # # # # # # # # # # # #
      ===
      ++++++++
      H2
      ++++++++
      H3
```

FIG. 29

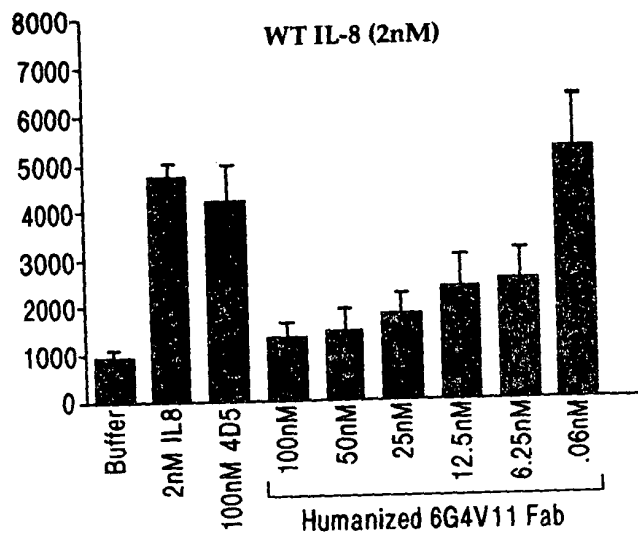


FIG. 30A

IC₅₀~12nM

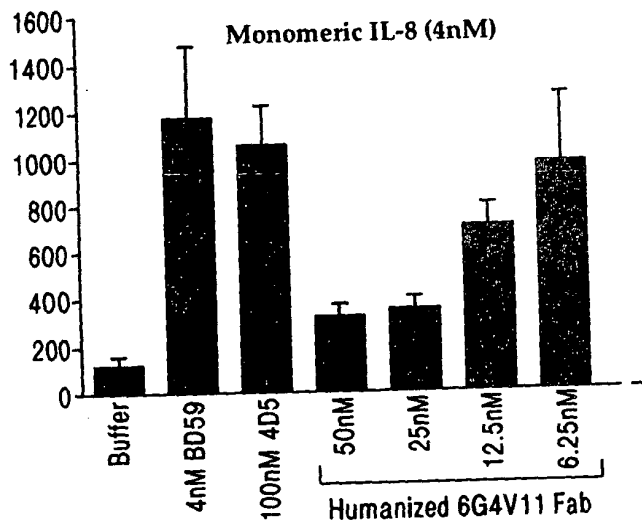


FIG. 30B

IC₅₀~15nM

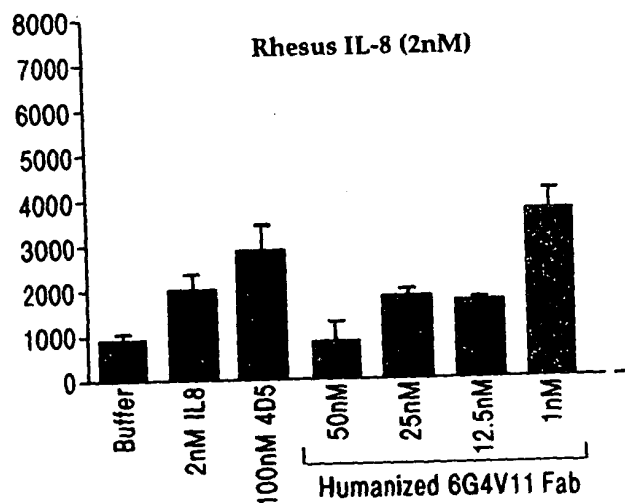


FIG. 30C

IC₅₀~22nM

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISSLQPEDFATYYCSQST
HVPITFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLVGVYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFDFVWGQGLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGGDFDYEKMANANKGAMTENADENALQSDAKGKLDVATDYGAIDFGIDVS
GLANGNGATGDFAGSSNSQMAQVGDGDN SPLMNNFRQYLPQLPQSVECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYVATFMYVFTFANILRNKES (SEQ ID NO.53)

FIG. 31A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTTCCTAT TGCTACAAAC
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
TCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G N T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT CCTGTCTGTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTTCCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TCGGCCTGCT GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.51)

FIG. 31B

FIG. 31B

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISLQPEDFATYYCSQST
HVPLTEGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVKQAPGKGLEWVGVIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.55)

FIG. 31C



FIG. 32

FORM 3-60 3-60 3-60 3-60 3-60

FIG. 32
CLASS

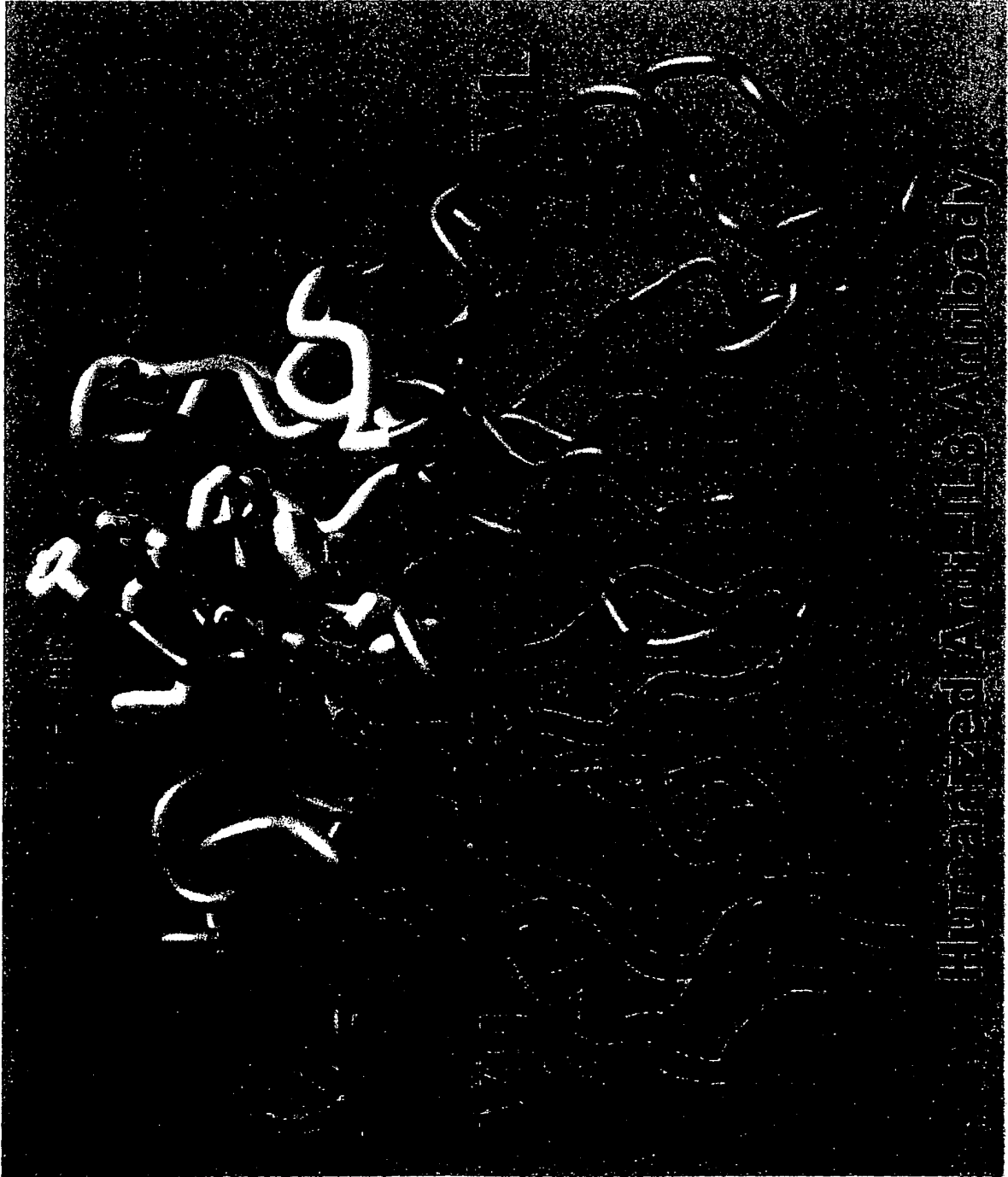


FIG. 32

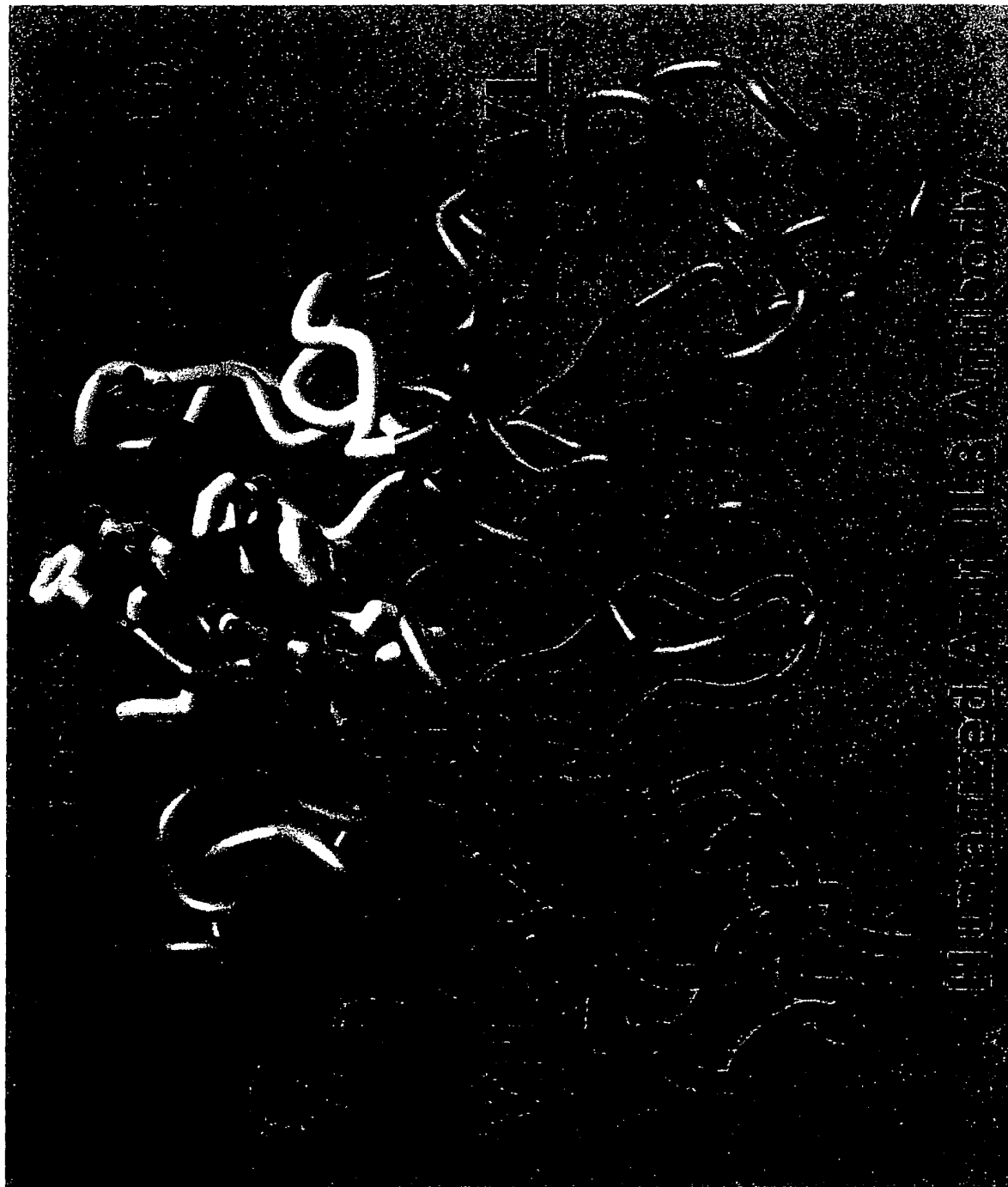


FIG. 32

FIG. 33

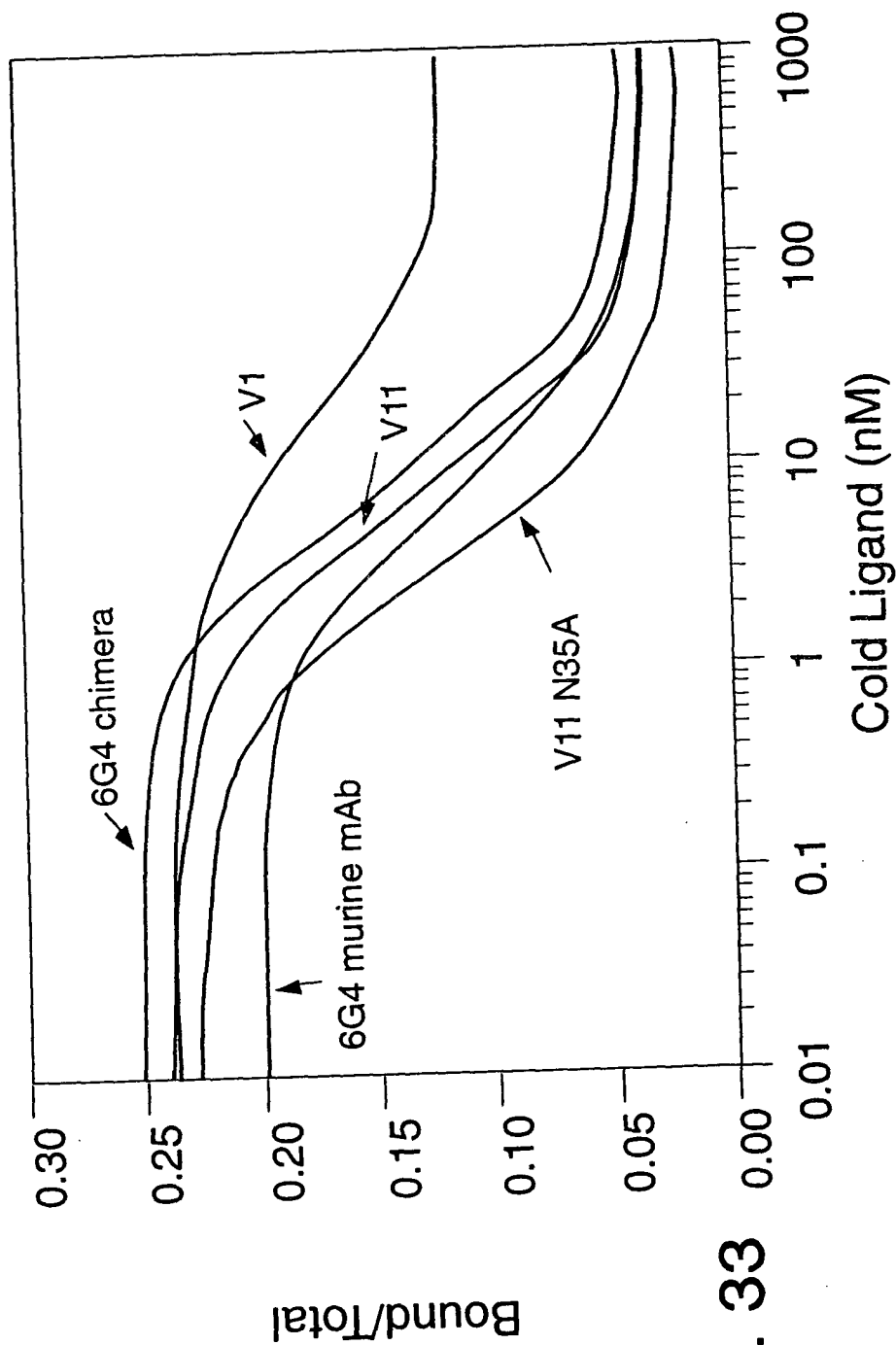
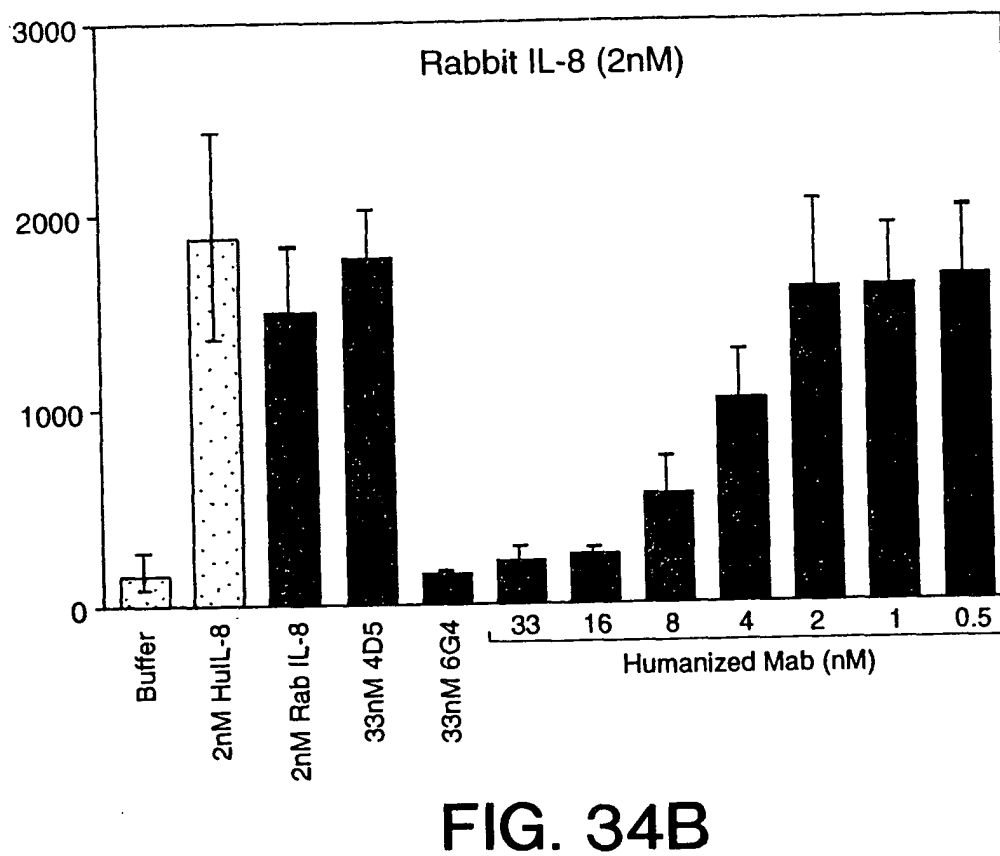
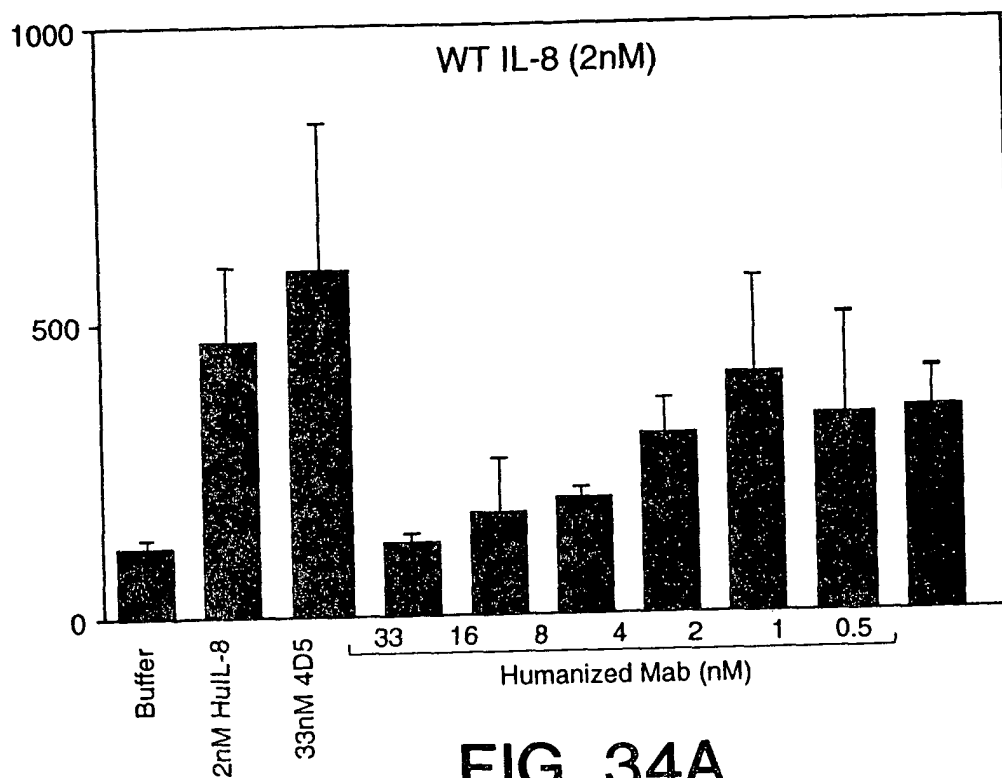
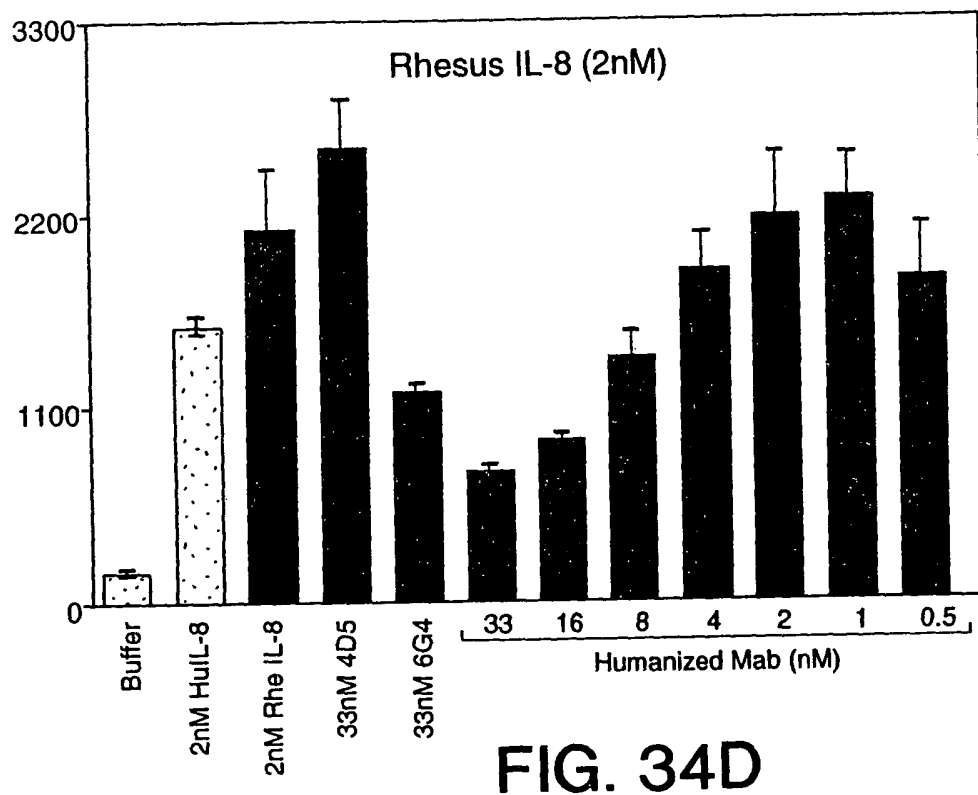
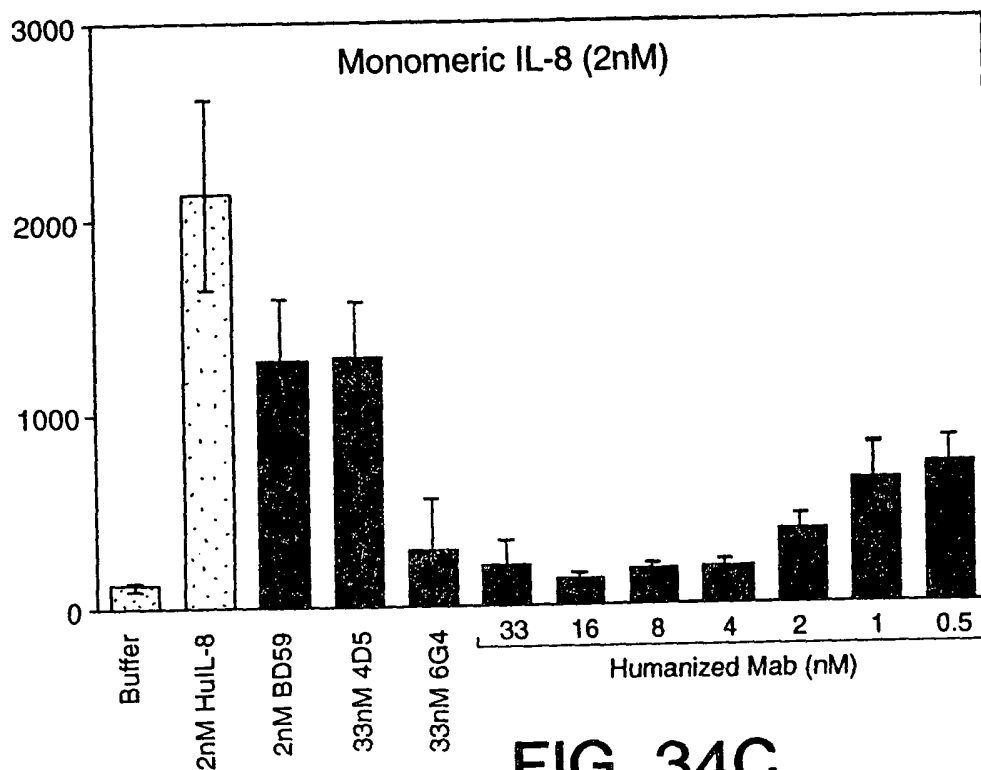


FIG. 33





Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGATY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISSLPEDFATYYCSQST
HVPLTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.56)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLWVGYYIDPSNGETTYNQKFGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTFSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELLGGRMKQLEDKVEELL SKNYHLENEVARLKKLVGER (SEQ ID NO.57)

FIG. 35

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S O S L V H G I G A T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCTA CAGTGTCTCG TCCTGTCTGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.56)

FIG. 36

0972055-053101

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTTCG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACATATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGCTCA TTTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCTTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTTCG GGTGCTGTGT GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA
TGAGTGTGTA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTGAT
228 T H T C P P C P A P E L L G G R M K Q L

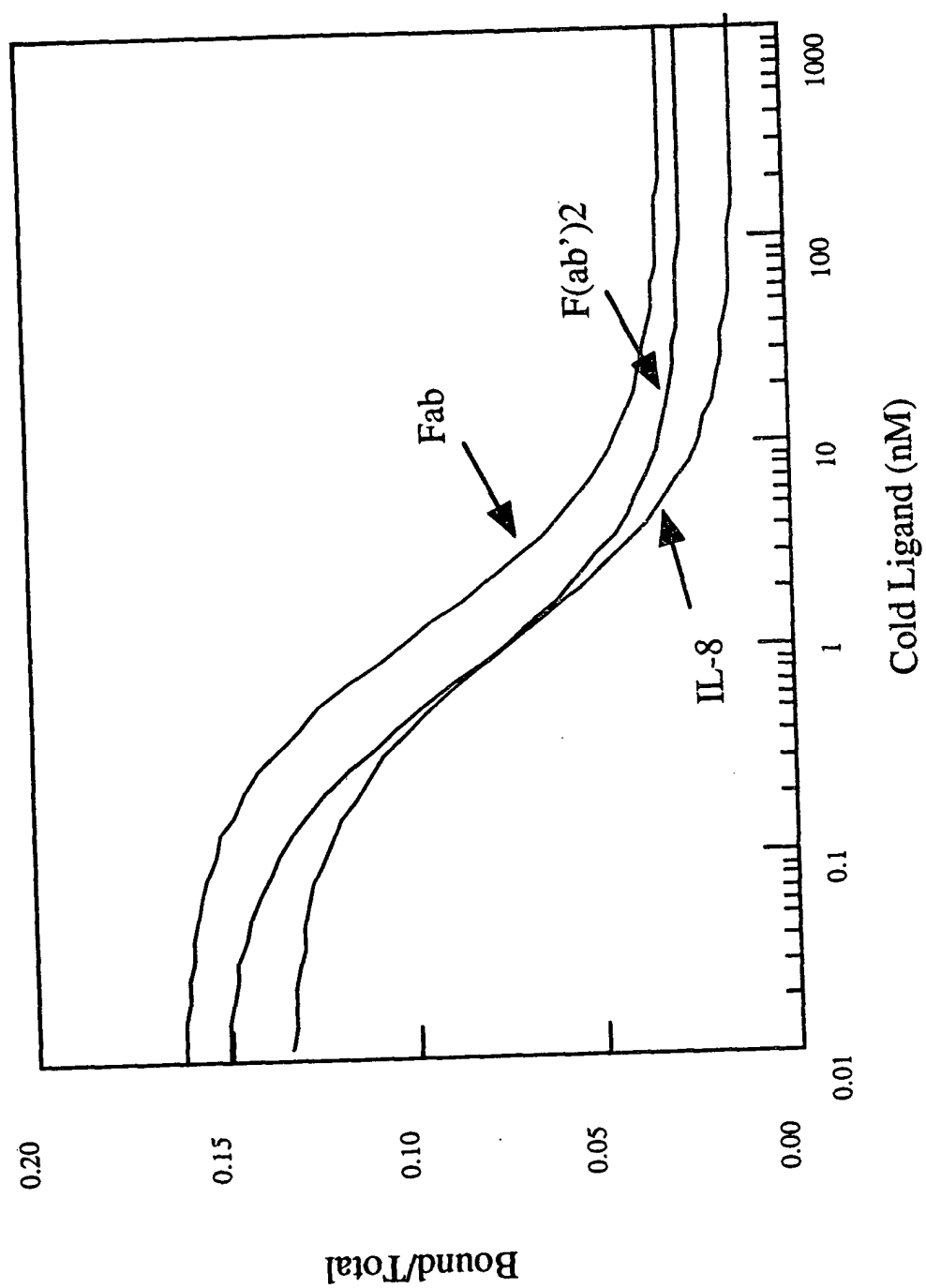
FIG. 37A

FIG.
SUBCLASS

1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTT TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (SEQ ID NO.59)
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O (SEQ ID NO.60)

FIG. 37B



ॐ
ॐ
ॐ
ॐ
ॐ

FIG. 39

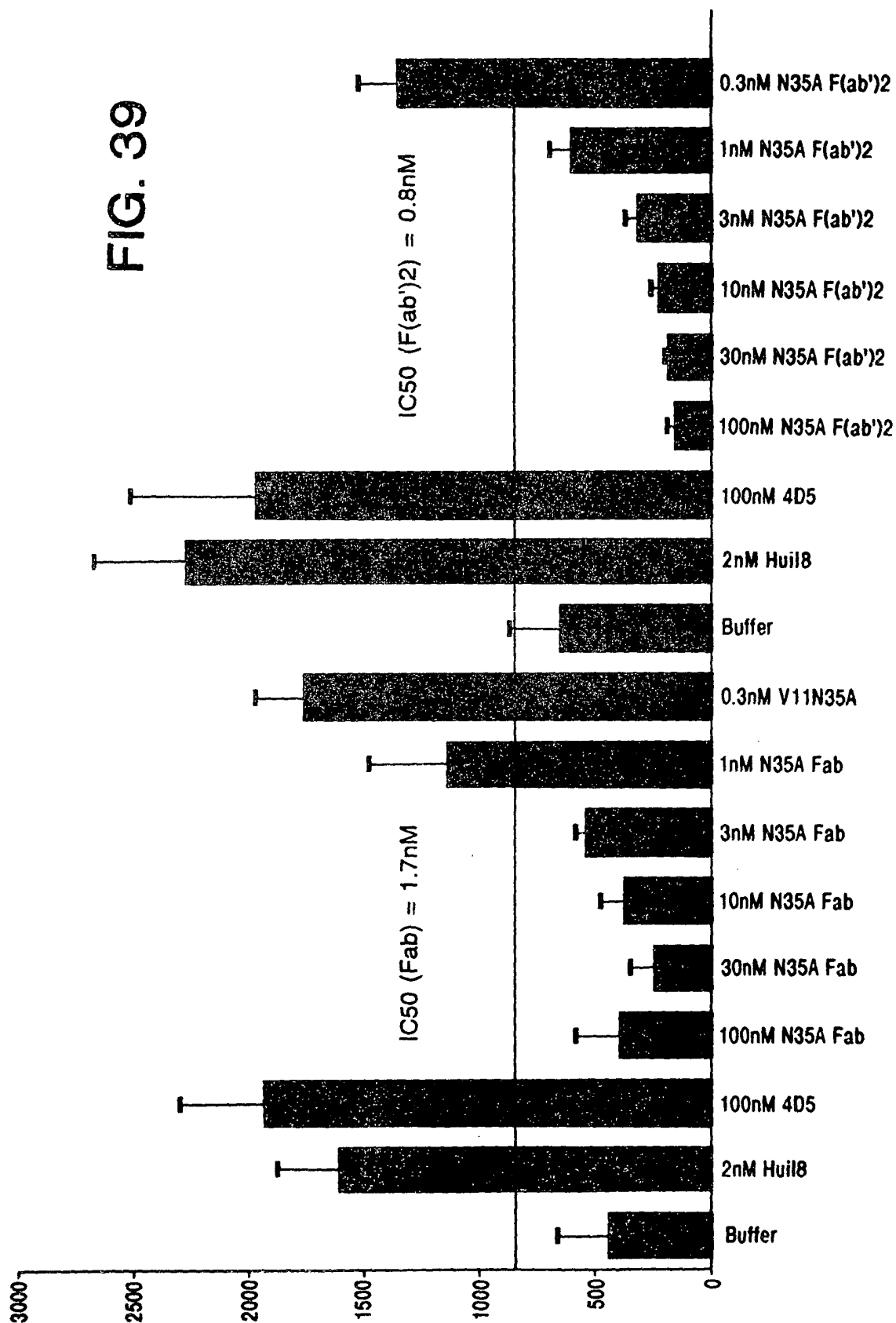


FIG. 40

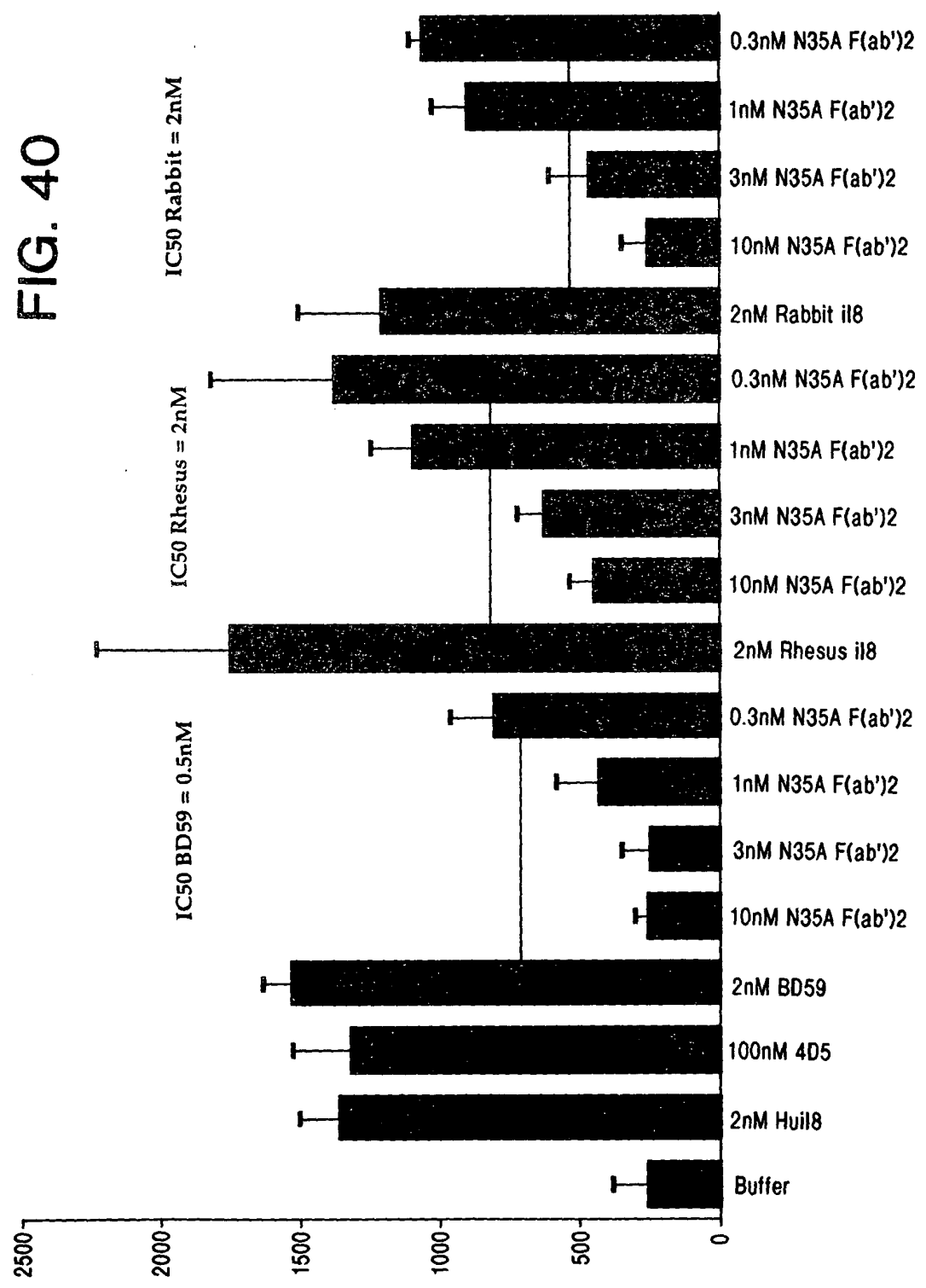


FIG. 41A

FIG. 41B

scrFI
ncII
mspi
hpaiI
dsav
xmaI/pspAI
smaI
scrFI
ncII
dsav
cauII
bsaJI
avaI
sau3AI taqI
rsaI mboI/ndeII{dam-}
csp6I dpaI{dam+}
nlaIV nlaIV paeR7I
kpnI cauII dpaII{dam-}
hgiCI bstYI/xhoII
bani bsaJI alwI{dam-}
asp718 bamHI avaI hphI
acc65I alwI{dam-} mnlI mnlI
401 TCGGTACCCG GGGATCCTCT CGAGGTTGAG GTGATTTTAT GAAAGAAT ATCGCATTC TTCTTGCATC TATGTTCTGT TTTTCTATTG CTACAACGC
AGCCATGGC CCTAGGAGA GCTCCAACCTC CACTAAATA CTTTCTTA TAGGTAAG AAGAAGCTAG ATACAAGCAA AAAAGATAAC GATGTTGCG
M K K N I A F L L A S M F V F S I A T N A
a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G to T ^

-23

ecorV
501 ATACGCTGAT ATCCAGATGA CCCAGTCCOC GAGCTCCTG TCCGCTCTG TGGCGATAG GGTCAACCATC ACCTGCAGGT CAAGTCAAG CTTAGTACAT
TATCGGACTA TAGGTCTACT GGGTCAGGGG CTCGAGGGAC AGGCGGAGAC ACCGCTATC CCAGTGGTAG TGGACGTCCA GTTCAGTTTC GAATCATGTA
-2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H

bsmFI bmyI
bsrI avaI aluI
tth111I/aspi baniI
ecorV
bspMI
scfI
psti
hphI
maeIII
bstEII hphI bsgI
sse8387I
dcl
nlaIII
aluI
rsaI
hindiIII
csp6I
CAAGTCAAG CTTAGTACAT
GTTCAGTTTC GAATCATGTA

FIG. 41B

FIG. 41C

1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGTA CGCTGAGCAA AGCAGACTAC GAGAACACA AAGTCTACGC

901 TCTGGAAGTG CTCTGTGTGT GTGCTGTCTG AATACTTCT ATCCAGAGA GCCCAAAGTA CAGTGGAGG TGGATAAGC CCTCCAATCG GGTAACTCCC
AGACCTTGAC GAAGACAACA CACGGAGGAC TTATTGAAGA TAGGGTCTCT CCGGTTTCAT GTCACCTTCC ACCTATTGCG GGAGGTAGC CCATTGAGG
132 S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q

1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGTA CGCTGAGCAA AGCAGACTAC GAGAACACA AAGTCTACGC
TCCTCTCACA GTGCTCTGTC CTGTCTGTC CTGTCTGTC GTGCTGTC GTGCTGTC GTGCTGTC GTGCTGTC GTGCTGTC GTGCTGTC GTGCTGTC GTGCTGTC
166 E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A

cac8I
alul
ssti
saci
hgiJII
hgiAI/aspHI
ec1136II
bsp1286
bsiHRAI
bmyI

hphI
maeIII
CTGCGAAGTC ACCCATCAGG GCCTGAGTCC GCGGCTGAGT TTTCTGCAAGT TGTCCTCTCT CACAAATCGA CTAGGAGATG CGGCTGCGGT AGCACCGGGA
199 C E V T H Q G L S S P V T K S F N R G E C O (SEQ ID NO.56)

FIG. 41D

-23

scrFI
ncII
mspI
hpall
dsav
cauII
bsII
xmal/pspAI
smaI
scrFI
ncII
dsav
cgaII
bsII

scrFI
mvaI
ecoRII

FIG. 41E

FIG. 41E

FIG. 41G

FIG. 41H

fnu4HI
 bsoFI
 haeIII/palI
 mcrI
 eagI/xmaIII/ecI XI
 eaeI
 cfrI
 bsiEI
 notI
 fnu4HI
 bsoFI
 nlaIII
 acII acII
 aluI mnlI
 rmaI
 maeI
 bfaI
 tthlIII/aspI
 taqI
 aluI
 sapi
 mboII
 earI/ksp632I
 rmaI
 maeI
 bfaI
 2001 TCACACATGC CCGCGTGGC CAGCACCAGA ACTGCTGGC GCGCGATGA AACAGCTAGA GGAAGAAGTC GAAGAGCTAC TCTCCAGAA CTACCACCTA
 AGTGTGTACG GCGGCACGG GTGCTGGTCT TGACGACCG CCGCGTACT TTGCTGATCT CCGTGTCCAG CTCTCGATG AGAGTTCTT GATGTTGAT
 229 H T C P C P A P E L G R M K Q L E D K V E E L S K N Y H L
 ^junction between antibody and leucine zipper

scrFI
 nclI
 mspI
 hpaII
 dsav
 caulI
 acII
 fnu4HI
 bsoFI
 sphI
 ddeI nlaIII
 celII/espI
 b1pI/bp1102I
 hinPI nspI
 hhaI/cfoI
 haeII nspHI
 eco47III cac8I
 CGACGGCCCT AGAGTCCCTA AGCTCGGT GCGCGCGGC GTTTTNTT
 CTCTTACTC ACCGTCTGA GTTTTCGA CAGCCCTCG CGATTCTAC TCTCAGGAT TCGAGCCAA CCGCGGCCG CAAAAATAA
 262 E N E V A R L K K L V G E R O (SEQ ID NO.60)

tru9I
 msel
 hpaI nlaIII
 hincII/hindII
 2201 GTTAATCAT GTTGACAGC TTATCATGA TAAGCTTTAA TCGGGTAGT TATCAGATT AAATGTCTAA CCGAGTCAG CACCGTGTAT GAAATCTAAC
 CAATTGACTA CAACTGTGC AATAGTAGCT ATTGAAATT ACGCCATCA ATAGTCTCA TTTAAGGATT GGTTCAGTCC GTGGCACATA CTTTAGATTG

FIG. 41H

FIG. 41I

FIG. 41J

FIG. 41K

FIG. 1

3201 CCCATTATGA TTCTTCTCGC TTCCGGCGGC ATCGGGATGC CCGCGTTGCA GGCCATGCTG TCCAGGCGAGG TAGATGACGA CCATCAGGGA CAGCTTCAAG bsmFI aluI alwI[dam-]
GGTAATACT AAGAAGACG AAGCGCGCG TAGCCCTACG GCGCAACGT CCGGTACGAC AGTCCGCTCC ATCTACTGCT GGTAAGTTC

3301 GATCGCTCGC GGCTCTTACC AGCCTAACTT CGATCACTGG ACCGCTGATC GTCACGGCGA TTTATGCCGC CTCGGCGAGC ACATGGAACG GGTGGCATG
CTAGCGAGCG CCGAGATGG TCGGATTGAA GCTAGTGACC TGGCGACTAG CAGTGCCGCT AAATACGGCG GAGCCGCTCG TGTACTTGC CCAACCGTAC

3401 GATTGTAGC GCGGCCCTAT ACCTTGTCTG CTCTCCCGCG TTGGTCCG GTGCATGGAG CCGGCCACCG TCGACTGAA TGAAGCCCG CGGCACCTCG
CTAACATCCG CCGCGGGATA TGAACAGAC GGAGGGCGC AAGCAGCGC CACGTACCTC GCGCCGCTG AGCTGACTT ACCTTGGCC GCGTGGAGC

FIG. 41L

FIG. 41M

```

sau3AI
mboI/ndeII{dam-}
mamI{dam-}
dpuI{dam+}
dpuII{dam-}
bstYI/xhoII
alwI{dam-}
mspI
hpaiI
mroI bsaBI{dam-} fnu4HI
bspMI
bspEI{dam-} bsoFI
bsaWI sfaNI bsvI
accIII{dam-} sfaNI
cac8I foki cac8I
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGGTACC
AATACAAGGC CTAGACGTAG CGTCCTACGA CGACCCGATGG
3801 TGGTCTTCGG TTCCGTGTT TCGTAAAGTC TGGAAACGCG GAAGTCAGCG CCCTGCACCA
ACCAAGAGCC AAAGGCACAA AGCATTTTCAG ACCTTTGGCG CTTCACTGCG GGGACGTGGT
acII
thai
fnuDII/mvni hinPI
bstUI hhaI/cfoI
bsh1236I haeII mslI
TGAAAGTC TCGTAAAGTC TGGAAACGCG GAAGTCAGCG CCCTGCACCA
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGGTACC
AATACAAGGC CTAGACGTAG CGTCCTACGA CGACCCGATGG
3901 CTGTGGAACA CCTACATCTG TATTAACGAA CGCGTGGCAT TGACCCCTGAG TGATTTTCT
GACACCTTGT GGATGTAGAC ATAATTGCTT CGGACCGTA ACTGGGACTC ACTAAAAAGA GACCAGGGCG CGGTAGGTAT GCGGTCAAC AAATGGAGT
cac8I foki
hinPI sfaNI
hhaI/cfoI nlaIV aciI
tru9I haeII avaiI fnu4HI bsri
mseI eco47III asuI bsoFI aciI mnlI
CTGTGGAACA CCTACATCTG TATTAACGAA CGCGTGGCAT TGACCCCTGAG TGATTTTCT CTGGTCCGC CGCATCCATA CCGCCAGTTG TTTACCCCTCA
GACACCTTGT GGATGTAGAC ATAATTGCTT CGGACCGTA ACTGGGACTC ACTAAAAAGA GACCAGGGCG CGGTAGGTAT GCGGTCAAC AAATGGAGT
4001 CAAAGTTCCA GTAACCGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCTCTCT CTGTTTCATCG GTATCATTAC CCGCATGAAC AGAAATTCOC
GTTGCAAGGT CATGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGG
bsri mnlI
bsli hpaII foki
maeII cauII
psp1406I maeIII nspHI sfaNI
CAAAGTTCCA GTAACCGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCTCTCT CTGTTTCATCG GTATCATTAC CCGCATGAAC AGAAATTCOC
GTTGCAAGGT CATGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGG

```

FIG. 41N

TOP SECRET 000000000000

4801	GAACCCGAC AGGACTATAA AGATACCAGG CGTTTCCCC TGGAGCTCC CTCCTGGCT CTTCTGTTCC GACCTGCGG CTTACCGGAT ACCTGTCCGC CTTTGGGCTG TCCTGATATT TCTATGGTCC GCAAGGGGG ACCTTCGAGG GAGCAGCGA GAGGACNAGG CTGGGACGGC GAATGGCCTA TGGACAGGCG	scrFI mvaI mvaI ecorII dsav bstNI apyI[dcmt] bsaJI aluI mnlI hhaI/cfoI hspI fnu4HI hpaII bsoFI bsaWI aciI mspi
4901	CTTTCTCCCT TCGGGAAGCG TGGCGCTTTC TCATAGCTCA CGCTGTAGT ATCTCAGTTC GGTGTAGGTC GTTCGCTCCA AGCTGGGCTG TGTGCACGAA GAAAGAGGGA AGCCCTTCGC ACCGGGAAAG AGTATCGAGT GCGACATCCA TAGAGTCAAG CCACATCCAG CAAGCGAGGT TCGACCCGAC ACACGTGCTT	hinPI hhaI/cfoI haeII aluI scfI ddeI
5001	CCCCCGTTC AGCCCGACCG CTGGCGCTTA TCCGGTAACT ATCGTCTTGA GTCCAAACCG GTAAGACACG ACTTATCGCC ACTGGCAGCA GCCACTGGTA GGGGGGCAAG TCGGGCTGGC GACGCGGAAT AGGCCATTGA TAGCAGAACT CAGGTTGGG CATTCGTGTC TGAATAGCGG TGACCGTCGT CGGTGACCAT	fnu4HI bsoFI nspBII aciI hinPI mcri bbvI bsiEI hhaI/cfoI hpaII mspi bsaWI pleI hinfi cauII mspi hpall scrFI nciI dsav maeIII
5101	ACAGGATTAG CAGAGCGAGG TATGTAGGCG GTGCTACAGA GTTCTTGAAG TGGTGGCCTA ACTACGGCTA CACTAGAAGG ACAGTATTG GTATCTGGCG TGTCCTAATC GTCTCGCTCC ATACATCCGC CACGATGTCT CAAGAATTC ACCACGGAT TGATGCCGAT GTGATCTTCC TGTCATAAAC CATAGACGCG	bsli mnlI aciI scfI haeIII/pall haeI bfaI rmaI maeI

FIG. 41Q

5201 TCTGCTGAAG CCAGTTACCT TCGGAAAAG AGTTGGTAGC TCCTGATCCG GCAACAAAC CACGCTGGT TTTTGTGTTG CAAGCAGCAG
AGACGACTTC GGTCAATGGA AGCCTTTTC TCAACCATCG AGAAGTAGGC CGTTGTGTTG GTGGGACCA TCGCCACCA AAAACAAAC GTTCGTGTC

5301 ATTACGGCA GAAAAAGG ATCTCAAGAA GATCCTTTGA TCTTTCTAC GGGCTCTGAC GCTCAGTGA ACAGAACTC ACGTAAGG ATTTGGTCA
TAATGCGGT CTTTTTTC TAGAGTTCTT CTAGGAACT AGAAAGATG CCCAGACTG CGAGTACCT TGCTTTGAG TGCAATCCC TAAACCCAGT

5401 TGAGATTATC AAAAGGATC TTCACCTAGA TCTTTTAA TTAATAATGA AGTTTAAAT CAATCTAAAG TATATAGAG TAAACTGGT CTGACAGTTA
ACTCTAATAG TTTTCTCTAG AAGTGGATCT AGGAAATTT AATTTTACT TCATAATTTA GTTAGATTTC ATATATCTC ATTTGAACCA GACTGTCAAT

5501 CCAATGCTTA ATCAGTGAGG CACCTATCTC AGCGATCTGT CTATTCGTT CATCCATAGT TGCCTGACTC CCGCTGCTGT AGATACTAC GATACGGGAG
GGTTACCAAT TAGTCACTCC GTGGATAGAG TCGCTAGACA GATAAGCAA GTAGTATCA ACGGACTGAG GGGCAGCACA TCTATTGATG CTATGCCCTC

FIG. 41R

FIG. 1

bsrI sau96I fnu4HI fnuDII/mvni mspI hpaII haeIII/palI haeIII/hinPI
nlaIV bsoFI bsh1236I cfr10I/bsrFI hphI nlaIV cac8I sau96I hinPI
asuI bsvI aciI bsh1236I hphI nlaIV cac8I sau96I hinPI
601 GGCTTACCAT CTGGCCCCAG TGCTGCAATG ATACCGCGAG ACCACGCTC ACCGGCTCCA GATTATCAG CAATAAACCA GCAGCCGGA AGGCCGAGC
CCGAATGGTA GACCGGGTC ACAGCTTAC TATGGCGTC TGGGTGCGAG TGGCGAGGT CTAATAGTC GTTATTGGT CCGTGGCCT TCCGGCTCG

bsrI fnu4HI fnuDII/mvni mspI hpaII haeIII/palI haeIII/hinPI
nlaIV bsoFI bsh1236I cfr10I/bsrFI hphI nlaIV cac8I sau96I hinPI
asuI bsvI aciI bsh1236I hphI nlaIV cac8I sau96I hinPI
601 GGCTTACCAT CTGGCCCCAG TGCTGCAATG ATACCGCGAG ACCACGCTC ACCGGCTCCA GATTATCAG CAATAAACCA GCAGCCGGA AGGCCGAGC
CCGAATGGTA GACCGGGTC ACAGCTTAC TATGGCGTC TGGGTGCGAG TGGCGAGGT CTAATAGTC GTTATTGGT CCGTGGCCT TCCGGCTCG

bsrI fnu4HI fnuDII/mvni mspI hpaII haeIII/palI haeIII/hinPI
nlaIV bsoFI bsh1236I cfr10I/bsrFI hphI nlaIV cac8I sau96I hinPI
asuI bsvI aciI bsh1236I hphI nlaIV cac8I sau96I hinPI
601 GGCTTACCAT CTGGCCCCAG TGCTGCAATG ATACCGCGAG ACCACGCTC ACCGGCTCCA GATTATCAG CAATAAACCA GCAGCCGGA AGGCCGAGC
CCGAATGGTA GACCGGGTC ACAGCTTAC TATGGCGTC TGGGTGCGAG TGGCGAGGT CTAATAGTC GTTATTGGT CCGTGGCCT TCCGGCTCG

FIG. 41S

FIG. 41T

REF ID: A66926

6401 TTTGCTCATG AGCGGATACA TATTGATG TATTAGAA AATAACAA TAGGGTTCC GCGACATT CCGCAAG TGGCCTGA CGTCAAGAA
 AACAGAGTAC TCGCTATGT ATAACTTAC ATAACTTCTT TTATTGTTT ATCCCAAGG CGGTGTAA GGGCTTTTC ACGTGGACT GCAGATTCTT
 nlaIII rcaI bspHI acil
 bsaI bsrBI
 hinPI
 thal
 fnuDII/mvni
 bstUI
 bsh1236I
 aciI
 nlaIV hhaI/cfoI
 sau96I
 haeIII/palI
 asuI
 ecoO109I/draII
 mnlI
 bssSI
 bbsI
 nlaIII rcaI tru9I
 bspHI mseI
 6501 ACCATTATTA TCATGACATT AACCTATATA AATAGGCGTA TCACGAGGCC CTTTCGTCTT CAA (SEQ ID NO.61)
 TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGGCAT AGTGCTCCGG GAAAGCAGAA GTT
 mboII
 bpuAI
 maeII
 hnlII/acyI
 ahaII/bsaHI
 aatII ddeI

FIG. 41U

FIG. 41V

```
>length: 6563

aatII(GACGTC): 1645 6489
acc65I(GGTACC): 403 823
accI(GTMKAC): 1093 1963 4449
accII(TCCGGA): 3867[dam-]
acII(CCGC): 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
acyI see hinII
afIIII(ACRYGT): 1307 4678
ageI(ACCGGT): 1788
ahaII/bsaHI(GRCGYC): 1645 1813 2616 2637 2751 3408 6107 6489
ahaII/draI(TTTAAA): 5435 5454 6146
ahdI/eam1105I(GACNNNNNGTC): 346 5566
aluI(AGCT): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
5922
alw44I/snoI(CTGCAC): 1831 4494 4992 6238
alwI[dam-](GGATC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
6196 6214
alwNI[dcn-](CAGNNNNCTG): 1117 1385 5089
apaI(GGGCCC): 1695
apaLI/snoI(CTGCAC): 1831 4494 4992 6238
apoI(RAATTY): 1 391 4093
apyI[dcn+](CCWGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asnI/vsPI(ATTAAAT): 5742
asnI see aseI
asp700(GAANNNTTC): 905 930 4234 6166
asp718(GGTACC): 403 823
aspHI see hgiAI
aspi see tthlII
asuI(GGNCC): 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
```

FIG. 41V

FIG. 42

Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEQ ID NO.63)

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO.64)

FIG. 42

Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A

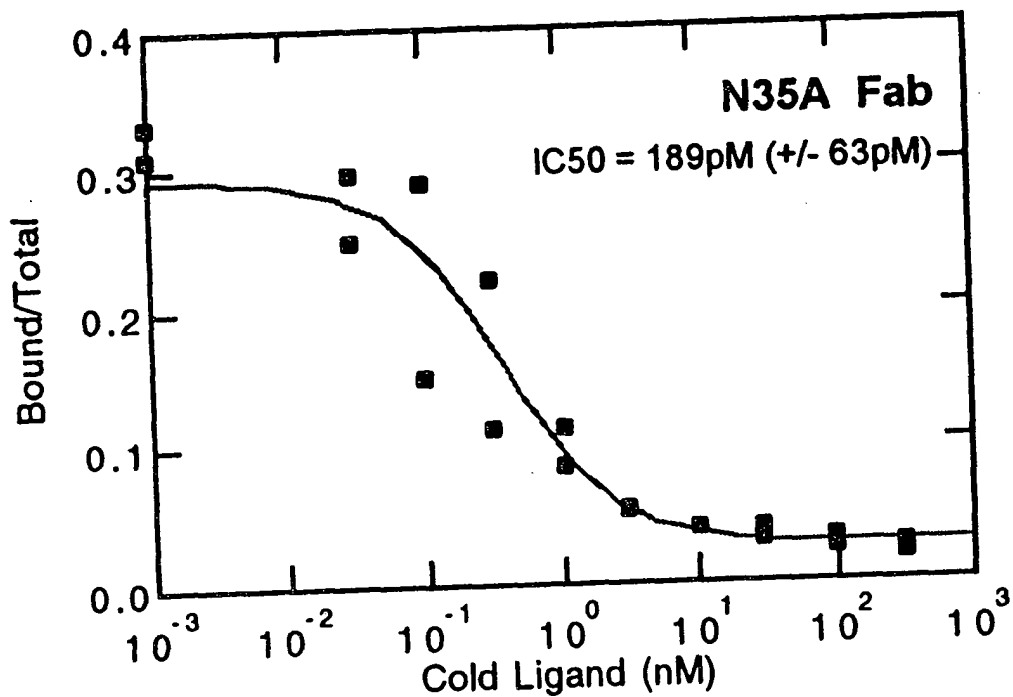


FIG. 43B

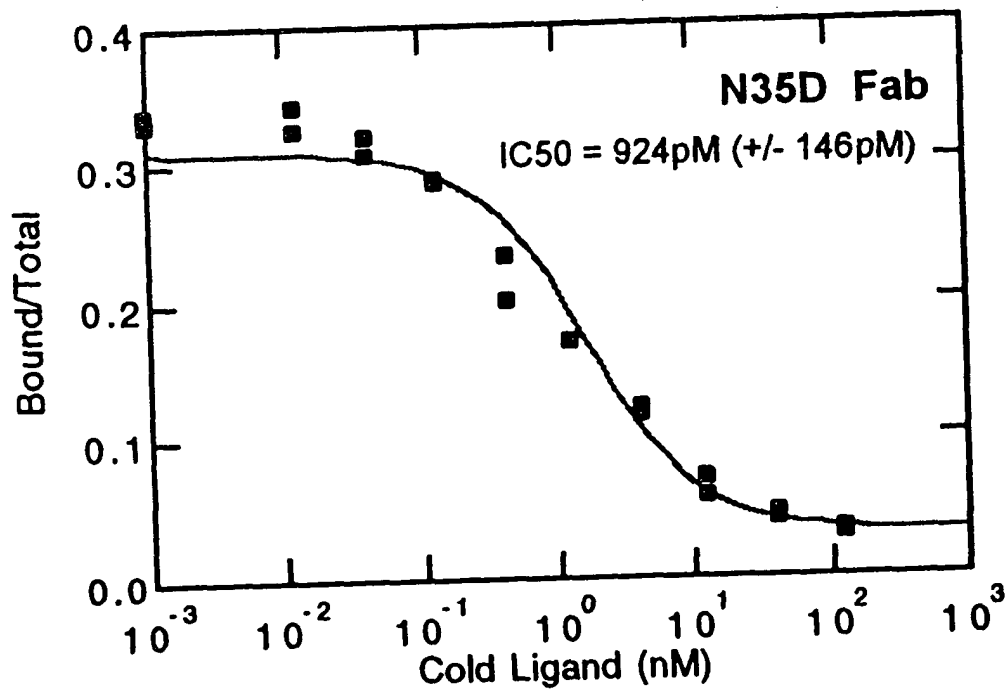


FIG. 43C

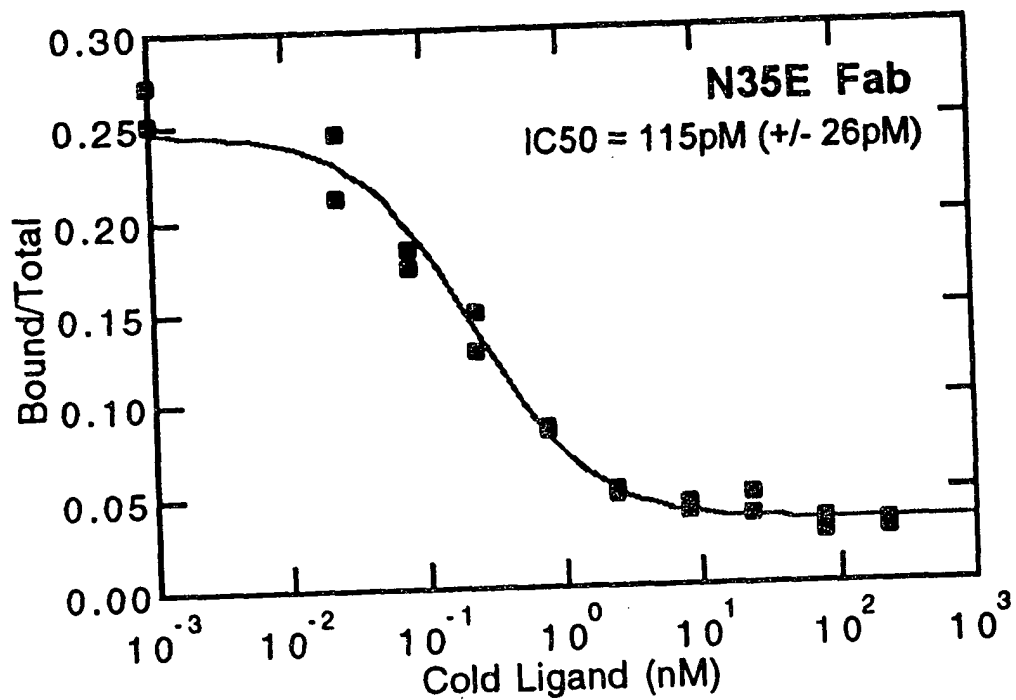


FIG. 43D

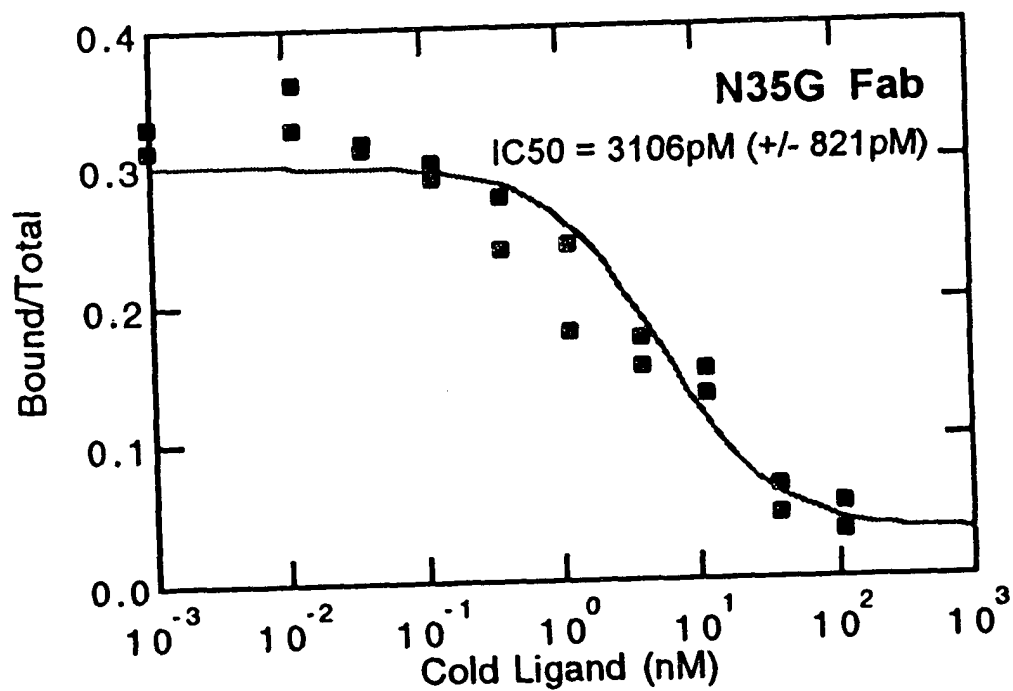
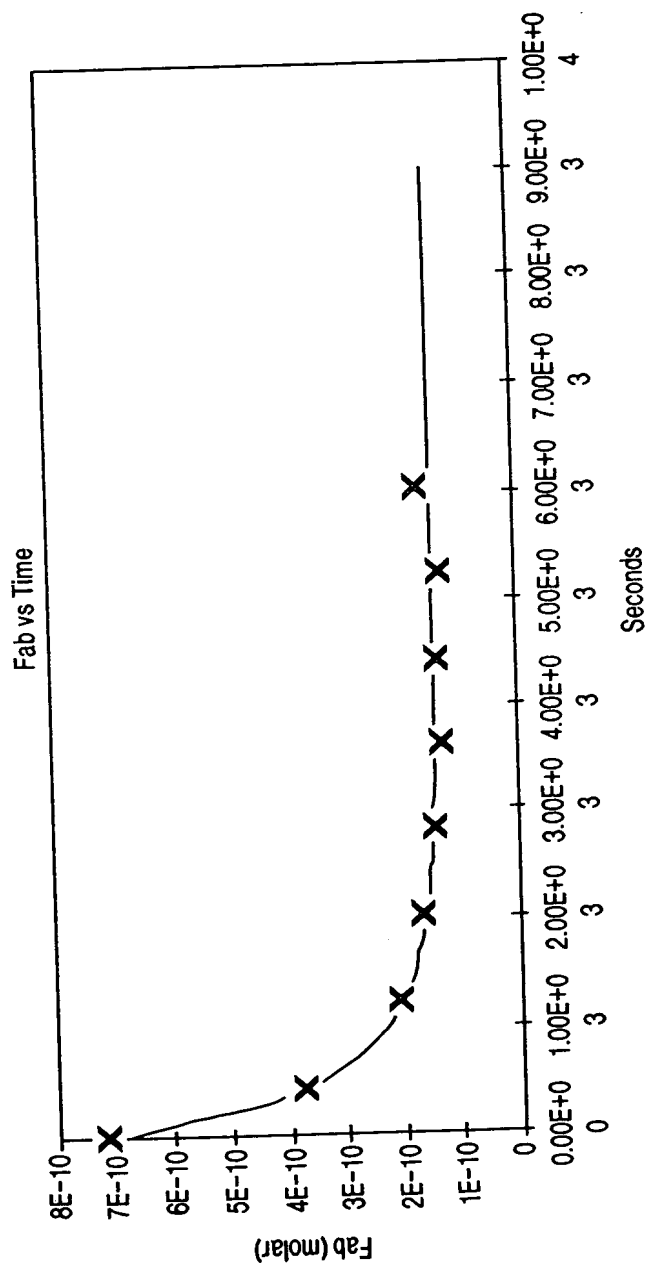


FIG. 43E



SAMPLE	k _a	k _d	K _d
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTTTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
18 R V T I T C R S S Q S L V H G I G E T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCAATTGAG GGTCCCTCTCA CAGTGTCTCG TCCTGTCTGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCCTCGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTG GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.62)

FIG. 45

FIG. 46

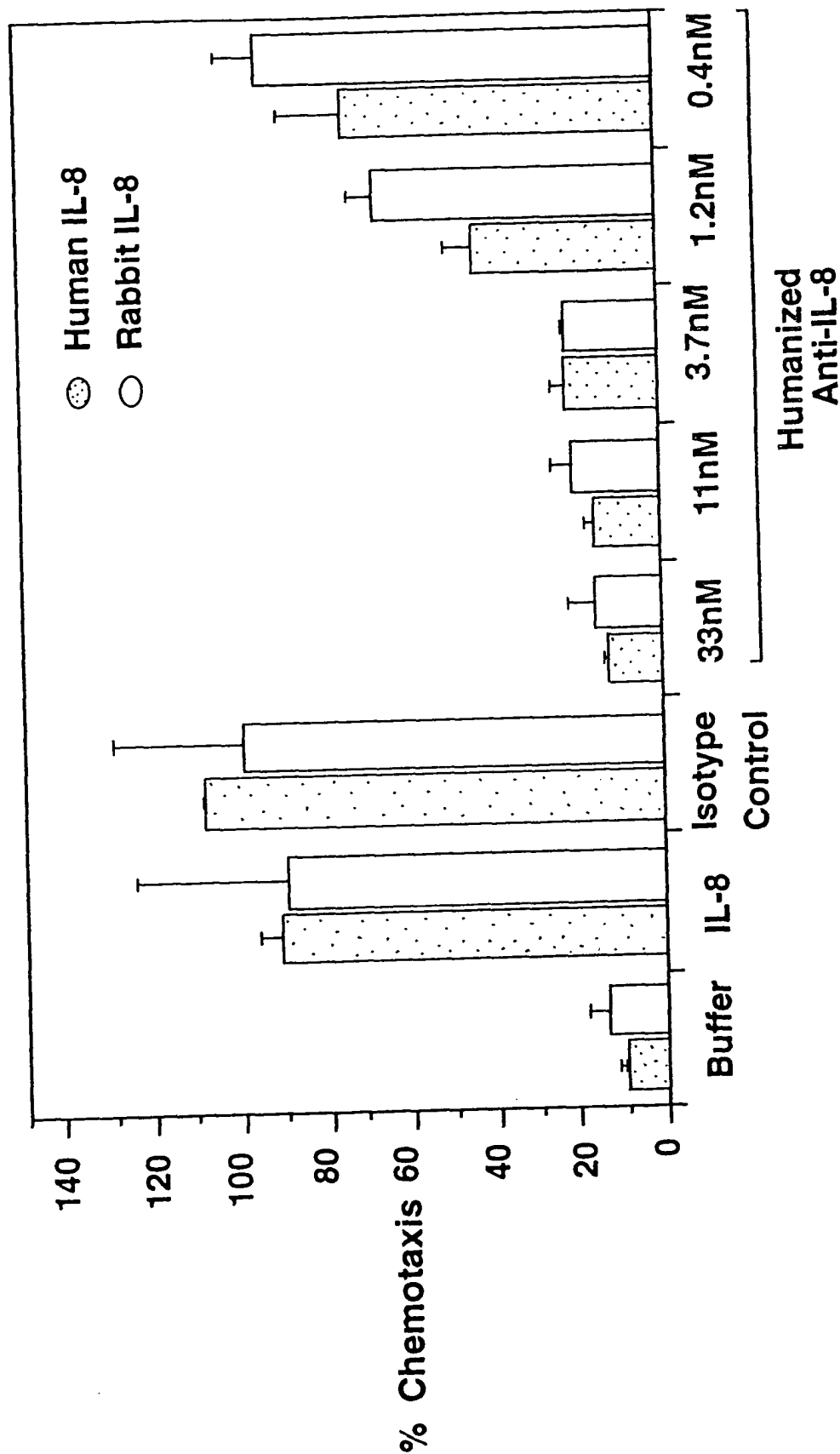


FIG. 46

TOP SECRET

APPROVED	FIG.
DRAFT	SUCCESS

N35AH1upr

5'-CTAGTGCAGTCTGGCGGTGGTGCAGCCAGGGGGCTACTCCGTTTGTCTGTGCAGCTTCTGGCTACTCCTTC-3'
(SEQ ID NO.66)

N35AH1lwr

5'-TCGAGAAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCACT
AG-3'
(SEQ ID NO.67)

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

>This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID)

This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intro made from pSVI.WTSD.D by adding a linearization linker(LL) into the HpaI site

[illegible][illegible]

FIG. 48A

FIG. 48B

FIG. 48C

601 CAAAGAAATGA CCACAACCTC TTCAAGTGGAA GGTAACACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCCTCCATTCC TGAGAGAAAT CGACCTTTAA
 GTTTCTTACT GGTGTTGGAG AAGTCACCTT CCATTGTCT TAGACCACCTA ATACCATCC TTTTGGACCA ACAGGTAAGG ACTCTTCTTA GTGGAAAT

eco57I mboII earI/ksp632I mnII tfII hinfI hphI alwNI[dcM-] apyI[dcM+] bstNI apyI[dcM+] sexAI ddel mboII taqI ahaII/draI
 mspI hpaII bsaBI accI nlaIII aacI nlaIII mnlI mspI hpaII bsaBI

701 AGGACAGAAAT TAATATAGT CTCACATAGAG AACTCAAGAG ACCACACAGA GGAGCTCATT TTCTTGCCAA AGTTTGGAT GATGCCITAA GACTTATTGA
 TCCGTCTTAA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGGTGGTGCT CCTCGAGTAA AAGAAGGTT TTCAAACCTA CTACGGGAAT CTGAATAACT

trn9I mseI aseI/asnI/vspI mnlI aluI bssI banII bslI bseRI bstXI foki sfanI mseI afnII/bfrI
 sstI sacI hglIII hgiAI/aspHI eclI36II bspI286 bsiHKA1 bmyI

801 ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTGTTGGATA GTCTGTGTTA CCAGGAGCC ATGAATCAAC CAGGCCACCT TAGACTCTTT
 TGTTGGCCTT AACCGTTTAT TTATCTCTGA CCAACCTAT CAGCTCCGT CAAGACAAAT GGTCTTCGG TACTAGTTG GTCCGGTGGA ATCTGAGAAA

haeIII/palI haeI

FIG. 48C

```
scrFI
mvaI
ecoRII
dsav
bstNI
apyI[d
sau96I
```

[illegible]

styI
 bsauI
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 alwI[dam-]
 bstyI/xhoII
 cac8I
 bsauI
 nlaIII
 styI
 ncoI
 dsaI bsmFI
 ppulOI
 nsII/avaIII
 ATAAGACCAT GGCACITTTT CTGGCTTTAG ATCCCTTTG CTTCTGTTAGA ACGCAGCTAC AATTAATACA TAACCTTTATG TATCATATAC
 TACGTAAAAA TATTCTGTA CCGTGAAAA GACCGAAATC TAGGGAAACC GAAGCAATCT TCGCTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG

sau96I
avaII
asuI
scrFI
mvaI
ecorII

FIG. 48D

[illegible]

FIG. 48E

FIG. 48F

bslI
 sau3AI
 mboI/ndeII[dam-]
 dpmI[dam+]
 dpmII[dam-]
 alwI[dam-]
 hphI
 cac8I mnlI
 ddelI drdI
 cac8I
 bspMI
 1501 ACCCTGCAGAT GAACAGGCTG CCGTCTGAGG ACACCTGCGT CTATTACTGT GCAAGAGGGG ATTATCGCTA CAATGCTGAC TGGTCTCTCG ACCTCTGGG
 TGGACGTCTA CTTGTGCGAC GCACGACTCC TGTGACGGCA GATAATGACA CGTCTCCTCC TAATAGCGAT GTTACCACTG ACCAAGAGGC TGCAGACCCC
 81 L Q M N S L R A E D T A V Y Y C A R G D Y R Y N G D W F F D V W G
 47 W V G Y I D P S N G E T T Y N Q K F K G R F T L S R D N S K N T A Y
 1701 TGGGTGGAT ATATTGATCC TTCCAATGCT GAACTACGT ATATCAAAA GTTCRAGGC CGTTTCACTT TATCTCGCGA CAATCCAAA AACACAGCAT
 ACCCAACCTA TATAACTAGG AAGGTTACCA CTTGATGCA TATTAGTTT CAAGTTCCCG GCAAAGTGAA ATAGAGCGCT GTTGAGGTTT TTGTGTCGTA
 114 Q G T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A
 hinII/acyI
 ahaiI/bsaHI
 aatII
 taqI
 bsri
 maeIII
 hphI
 mboII maeII
 scrFI
 mvaI
 ecorII
 dsav
 bstNI
 sau96I
 haeIII/pali
 asuI
 fnu4HI
 bsoFI
 bsp1286 aciI bsaJI
 bmyI nspBII apyI[dcn+]
 bmyI mnlI
 bmyI mnlI
 TCCACAGCA CCTCTGGGG CACAGCGCC
 AGTTCCTGG GACCACTGGC AGAGGAGCCG GAGGTGTTT CCGGTAGCC AGAAGGGGA CCGTGGAGG AGTTCCTGT GGAGACCCC GTGTCGCCG

FIG. 48F

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

1801 CTGGGCTGCC TGGTCAAGGA CTACTTCCCG GACCCGGTGA CGGTGTCGTG GAATCAGGC GCCTGACCA CGGGCGTGCA CACCTTCCCG GCTGTCCTAC
 GACCCGACGG ACCACTTCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCG CGGGACTGGT CGCGCACGT GTGGAAGGCG CGACAGGATG
 147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q
 1901 AGTCTCAGG ACTCTACTCC CTCAGCAGCG TGGTACTGT GCCCTTAGC AGCTTGGCA CCCAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA
 TCAGGAGTCC TGAGATGAGG GAGTCGTGCG ACCACTGACA CGGGAGATCG TCGAACCGT GGTCTGGAT GTAGAGCTTG CACTTAGTCT TCGGTCGTT
 181 S S G L Y S L S S V T V P S S S L G T Q T Y I C N V N H K P S N
 2001 CACCAAGGTG GACACAAAG TTGAGCCCAA ATCTTGTGAC AAAACTCACA CATGCCACCG GTGCCAGCA CCTGAACCTC TGGGGGACC GTCAGTCTTC
 GTGGTCCAC CTGTTCTTTC AACTGGGTT TAGAACACTG TTTTGTGTGT GTACGGGTGG CACGGGTGCT GACTTGGG ACCCCCTGG CAGTCAGAAG
 214 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 224 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 234 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 244 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 254 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 264 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 274 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 284 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 294 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 304 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 314 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 324 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 334 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 344 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 354 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 364 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 374 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 384 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 394 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 404 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 414 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 424 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 434 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 444 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 454 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 464 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 474 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 484 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 494 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 504 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 514 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 524 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 534 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 544 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 554 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 564 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 574 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 584 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 594 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 604 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 614 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 624 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 634 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 644 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 654 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 664 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 674 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 684 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 694 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 704 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 714 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 724 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 734 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 744 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 754 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 764 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 774 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 784 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 794 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 804 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 814 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 824 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 834 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 844 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 854 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 864 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 874 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 884 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 894 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 904 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 914 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 924 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 934 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 944 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 954 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 964 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 974 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 984 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 994 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F
 1004 T X V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F

FIG. 48G

acII
thai
fnuDII/mvni
bstUI
bsh1236I
sacII/sstII
nspBII
kspI
dsaI
bsaJI
maeII
rsaI
csp6I
bsrI bsaAI
acII
fnu4HI
bscFI
mnII
mnII
bseRI

[illegible]

FIG. 48H

FIG. 48I

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scrFI      nciI      mspI      hpaII      dsav      cauli
xmaI/pspAI
smaI      scrFI      nciI      dsav      cauli
rsal      foki
bslI      bsaJI      mboII
bspl407I/bsrGI      bslI      auaI      earI/kep632I
2401 CAGCCCCGAG AACACAGGT GTACACCGT CCCCCATCCC GGAAGAGAT GACCAAGAT CAGGTGAGCC TGACCTGCTT GGTCAAAGGC TTCTATCCCA
GTCGGGGGCTC TTGGTGCCA CATGTGGGAC GGGGGTAGGG CCCTTCTCTA CTGGTTCTTG CTCCAGTCGG ACTGGACGGA CCAGTTCCG AAGATAGGTT
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S

mspI      hpaII
fnu4HI      bsoFI      bsvI
bsrDI      bsaJI
2501 CGCAGATGCG CGTGGAGTGG GAGAGCAATG GGCAGCCGGA GAACAACATC AAGACCAGC CTCCCGTGGT GACTCCGAC GGCTCCTTCT TCCTCTACAG
CGCTGTAGCG GCACCTCACC CTCTCGTTAC CGTCGGGCTT CTGTGTGATG TTCTGGTGG GAGGGACAGA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC
381 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S

mboII      bpuAI      maelI      xmnI      bbsI      asp700      nlaIII      sfaNI      mnlI
fnu4HI      bsoFI      bsvI      bspMI      bbvI      bspMI      bbvI      bspMI      bbvI      bspMI      bbvI
414 K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L

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FIG. 48I

FIG. 48J

FIG. 48K

[illegible]

```

^U2 match
  lariat consensus^
IGG vH natural lariat restored^

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FIG. 48L

[illegible]

```

sau96I
avaII
asuI
scrFI
mvaI
ecoRII
dsav
bstNI
apyl[dcn+]
bslI bsaJI
          mnlI bsaJI nruI aluI
          bshl236I aluI
          bstUI cac8I
          fnu4HI
          fnuDII/mvnl
          fnu4HI
          bsoFI taqI apoI bslI foki
          bsvI bspDI[dam-] bsaJI
          GGGTGCATC GTTGAATTC CACCATGGGA
          CCCGACGTAG CTAACCTAAG GTGGTACCCT
          ^cloning linker
3501 CCACCTTTTC TTTTCTCCA CAGGTGTCCA CTCCCAGGTC CAACTGCACC TCGGTTCCGC AAGCTAGGTT
GGTCAAAAAG AAAAAGAGGT GTCCACAGGT GAGGGTCCAG GTTGACGTGG AGCCCAAGCG AGCCATCGAA

```

```

3601  TGGTCATGTA  TCATCCCTTTT  TCTAGTAGCA  ACTGCAACTG  GAGTACATTC  AGATATCCAG  ATGACCCAGT  CCCCAGCTC  CCTGTCCGCC  TCTGTGGCGG
      ACCAGTACAT  AGTAGGAAA    AGATCATCGT  TGACGTTGAC  CTCATGTAAG  TCTATGGTCA  TACTGGGTCA  GGGGTCGAG  GGACAGCGCG  AGACACCCGC
      D I O M T O S P S S L S A S V G D
      rmaI      mael      bmaI/gsuI[dcM-]  rsal      bsmFI  bmyI      bsri  avai      mniI
      foki      bfaI      bspI  csp6I      ecorV      tthlII/aspl  banII      aciI
      nlaIII
      aluI      ssti      sacI      hgiJII      hgiAI/aspHI      ecII36II      bspI286      bsiHKAI

```

[illegible]

FIG. 48M

FIG. 48N

FIG. 480

FIG. 48P

FIG. 48Q

FIG. 48B

FIG. 48S

FIG. 48T

FIG. 48U


```

sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-] thaI
mboI/ndeII[dam-] fnuDII/mvni
dpmI[dam+] dpmI[dam+] cac8I
dpmI[dam-] dpmI[dam-] bsh1236I fnu4HI
bstYI/xhoII alwI[dam-] hinPI bsoFI
alwI[dam-] bstYI/xhoII hhaI/cfoI bbvI
7101 TCAAAGGATC TTCTTGAGAT CCTTTTTC TGCGGTAAT CTGCTGCTG CAAACAAAAA AACACCGCT ACCAGCGTG GTTGTGTTGC CGGATCAAGA
AGTTTCCTAG AAGAACTCTA GGAATAAAG ACGGCATTA GACGACGAAC GTTGTGTTT TGGTGGCGA TGGTGGCGAC CAAACAAACG GCCTAGTTCT

sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-]
dpmI[dam+] dpmI[dam+]
dpmI[dam-] dpmI[dam-]
bstYI/xhoII alwI[dam-]
alwI[dam-] bstYI/xhoII
7201 GCTACCAACT CTTTTTCGA AGTAACCTG CTTACAGCAGA CGCAGATAC CAAATACTGT CCTGTAGTG TAGCCGTAGT TAGGCCACCA CTTCAAGAAC
CGATGGTTGA GAAAAAGGCT TCATTGACC GAAGTCGTCT CGCGTCTATG GTTATGACA GGAAGATCAC ATCGGCATCA ATCGGTGGT GAAGTTCTTG

sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-]
dpmI[dam+] dpmI[dam+]
dpmI[dam-] dpmI[dam-]
bstYI/xhoII alwI[dam-]
alwI[dam-] bstYI/xhoII
7301 TCTGTAGCAC CGCCTACATA CCTCGCTCTG CTAATCCTGT TACCAGTGGC TGCTGCCAGT GGGGATAAGT CGTGTCTTAC CGGTGGAC TCAAGACGAT
AGACATCGTG GCGGATGTAT GGAGCGAGAC GATTAGGACA ATGGTCACCG ACGACGGTCA CCGCTATTCA GCACAGAATG GCCCAACCTG AGTTCGTCTA

sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-]
dpmI[dam+] dpmI[dam+]
dpmI[dam-] dpmI[dam-]
bstYI/xhoII alwI[dam-]
alwI[dam-] bstYI/xhoII
7401 AGTTACCGGA TAAGCGCAG CGGTGGGCT GAACGGGGG TTCTGTGACA CAGCCAGCT TGGAGCGAAC GACCTACACC GAACCTAGAT ACCTACAGCG
TCAATGGCCT ATTCCGGCT GCGACCCGA CTTGGCCCCC AAGCAGCTGT GTCCGGTCCA ACCTCGCTTG CTGGATGCG CTTGACTCTA TGGATGCGC

```

FIG. 48W

FIG. 48X

FIG. 48Y

```
thai
fnduII/mvni
bstUI
bsh1236I
hinPI
hhaI/cfoI
thai
fnduII/mvni cac8I
bstUI haeIII/palI aluI
bsh1236I tru9I pvuII
mnlI bslI eaeI tfilI asei/asnI/vspI
aciI cfiI hinfI msei ne8BI
7901 CCGCCTCTCC CCGCGCGTTG GCGGATTAT TAATCCAGCT GGCAGGACAG GTTCCCGAC TGGAAAGCGG GCAGTGAGCG CAACGCAATT AATGTGAGTT
GGCGGAGAGG GGCGCGCAAC CGGCTAAGTA ATTAGGTGCA CCGTCTGTC CAAAGGGGTG ACCTTTCGCC CGTCACTCGC GTTCCGTTAA TTACACTCAA
scrFI
mvaI
ecorII
dsaV
nlaIV betNI
hgiCI apyI{dcm+} mspI aciI
banI bsaJI hpaII bsrBI aluI
8001 ACCTCACTCA TTAGGCACCC CAGGCTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGTG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACACGTA
TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAATATCGA AGGCCGAGCA TACAACACAC CTTAACACTC GCCTATGTT AAAGTGTGTC CTTTGTGAT
```

FIG. 48Y

FIG. 48Z

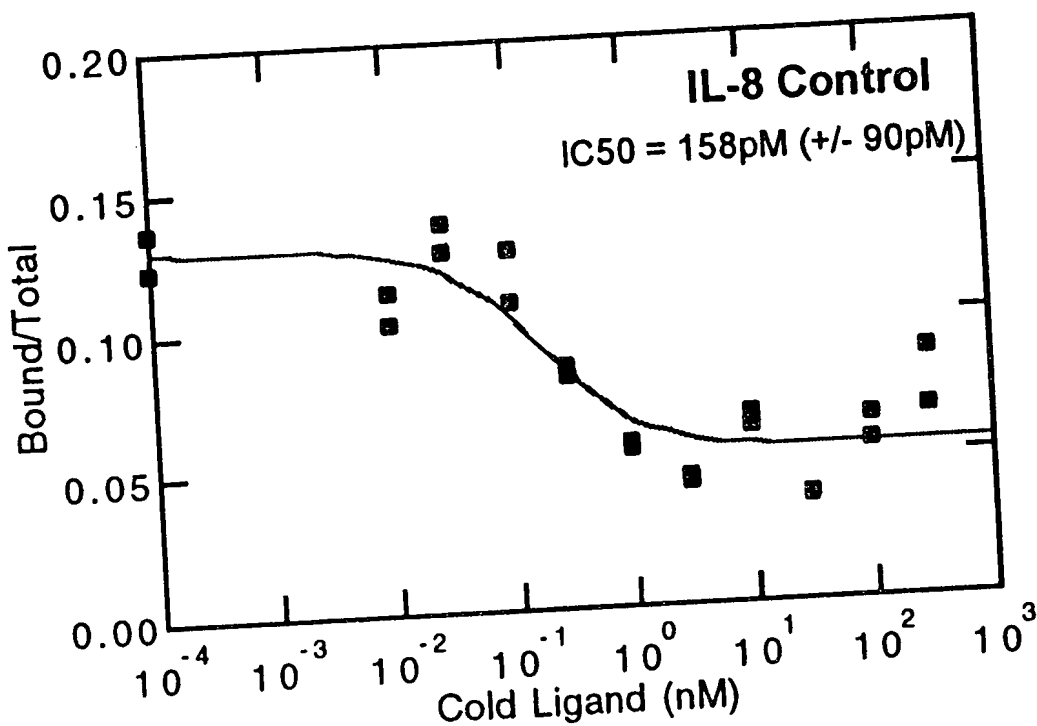


FIG. 49A

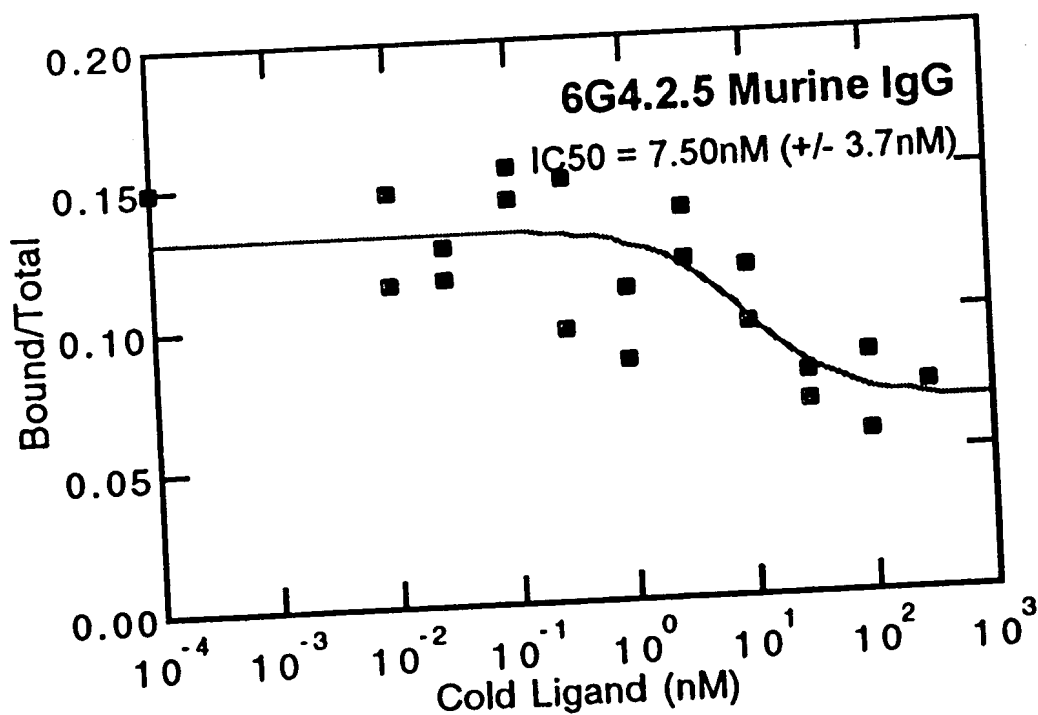


FIG. 49B

FIG. 49A

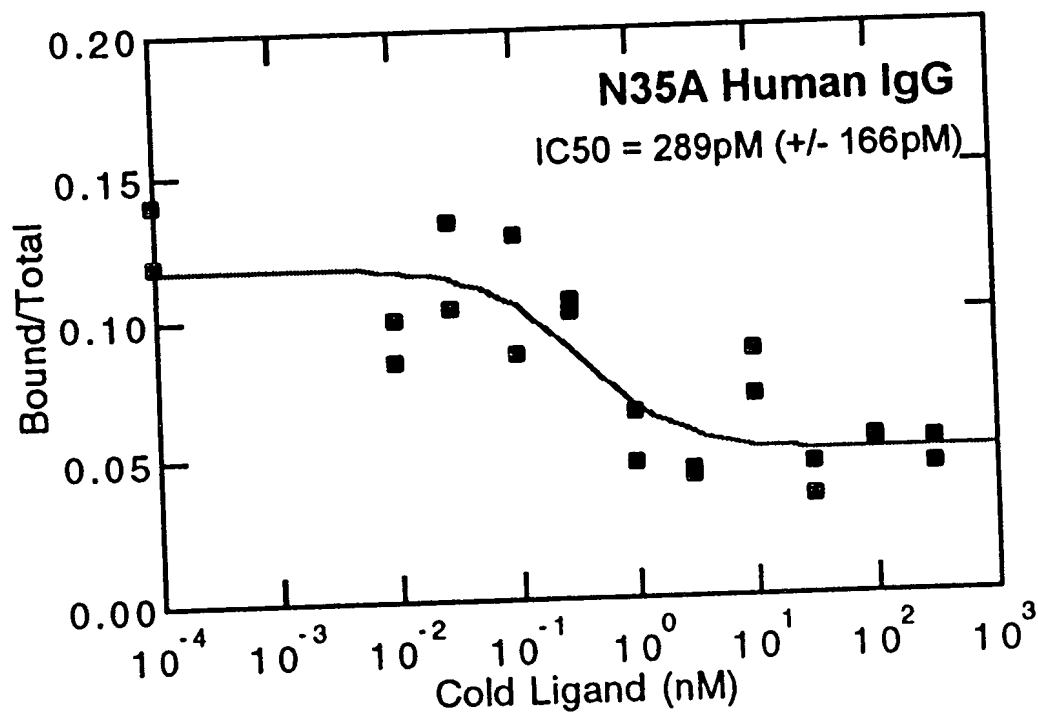


FIG. 49C

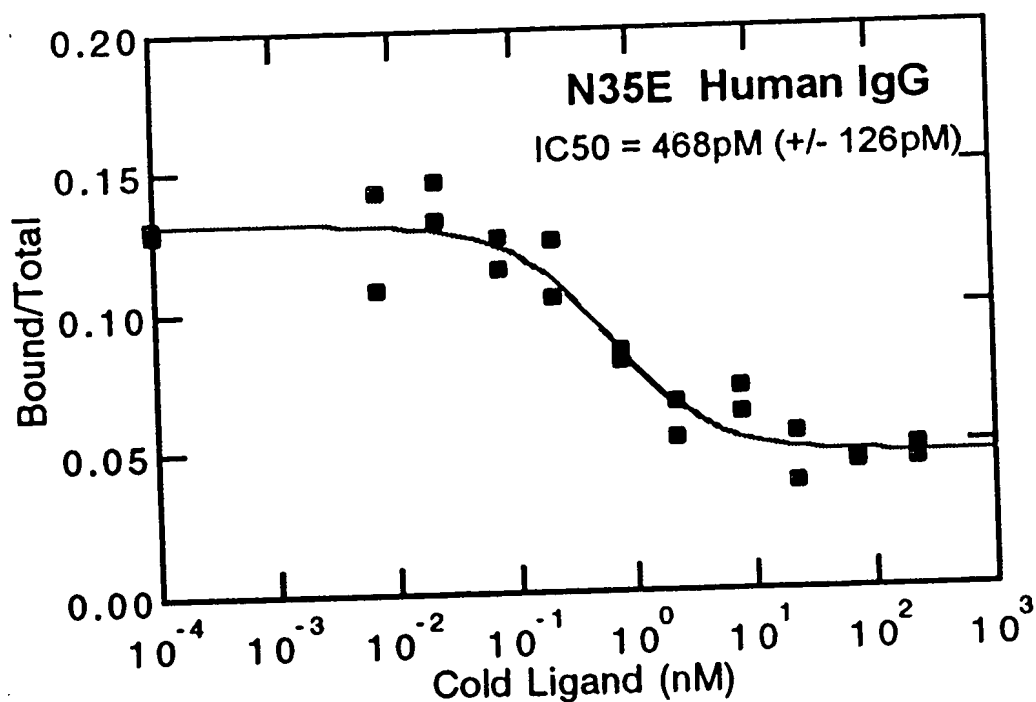


FIG. 49D

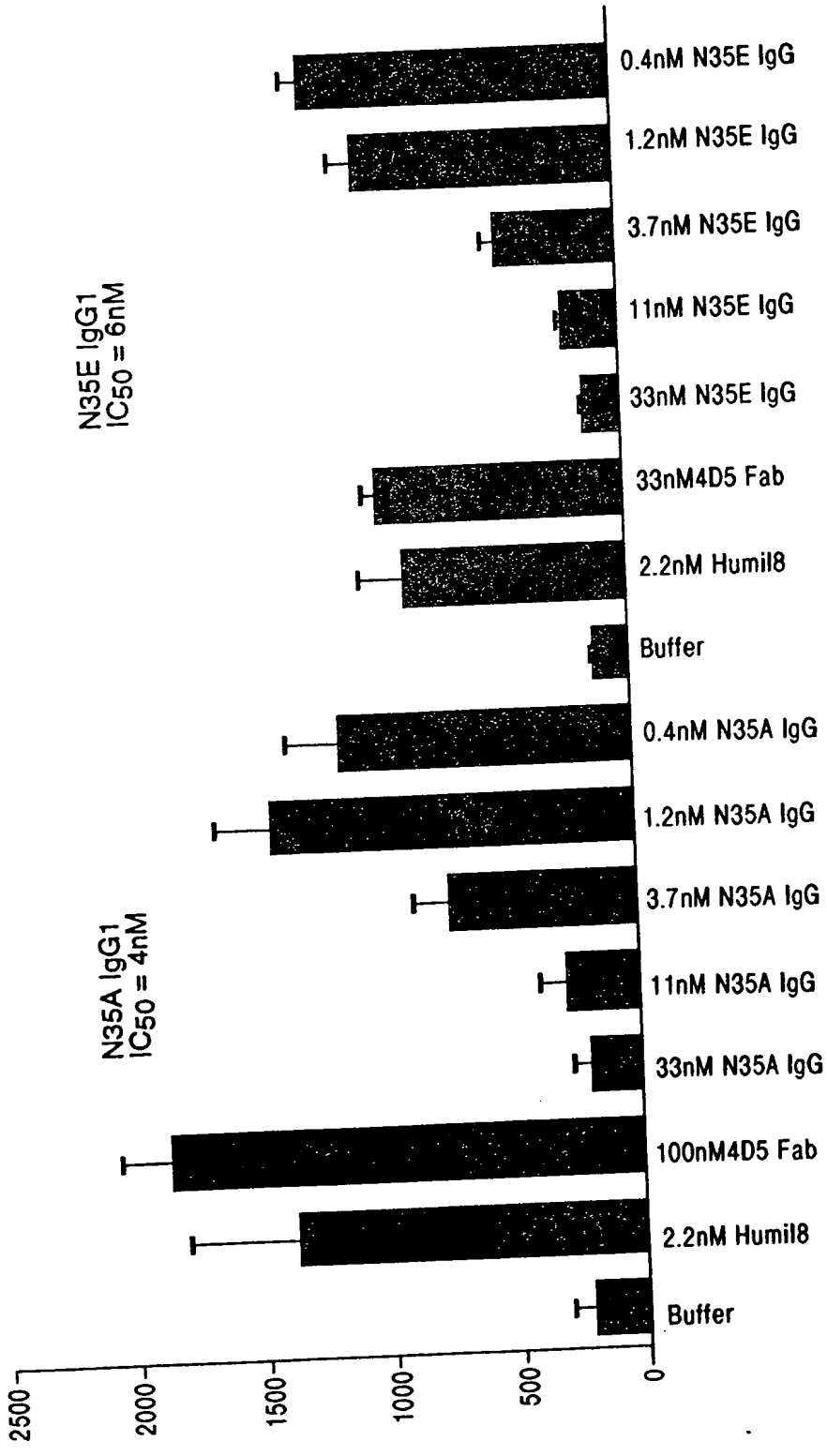


FIG. 50A

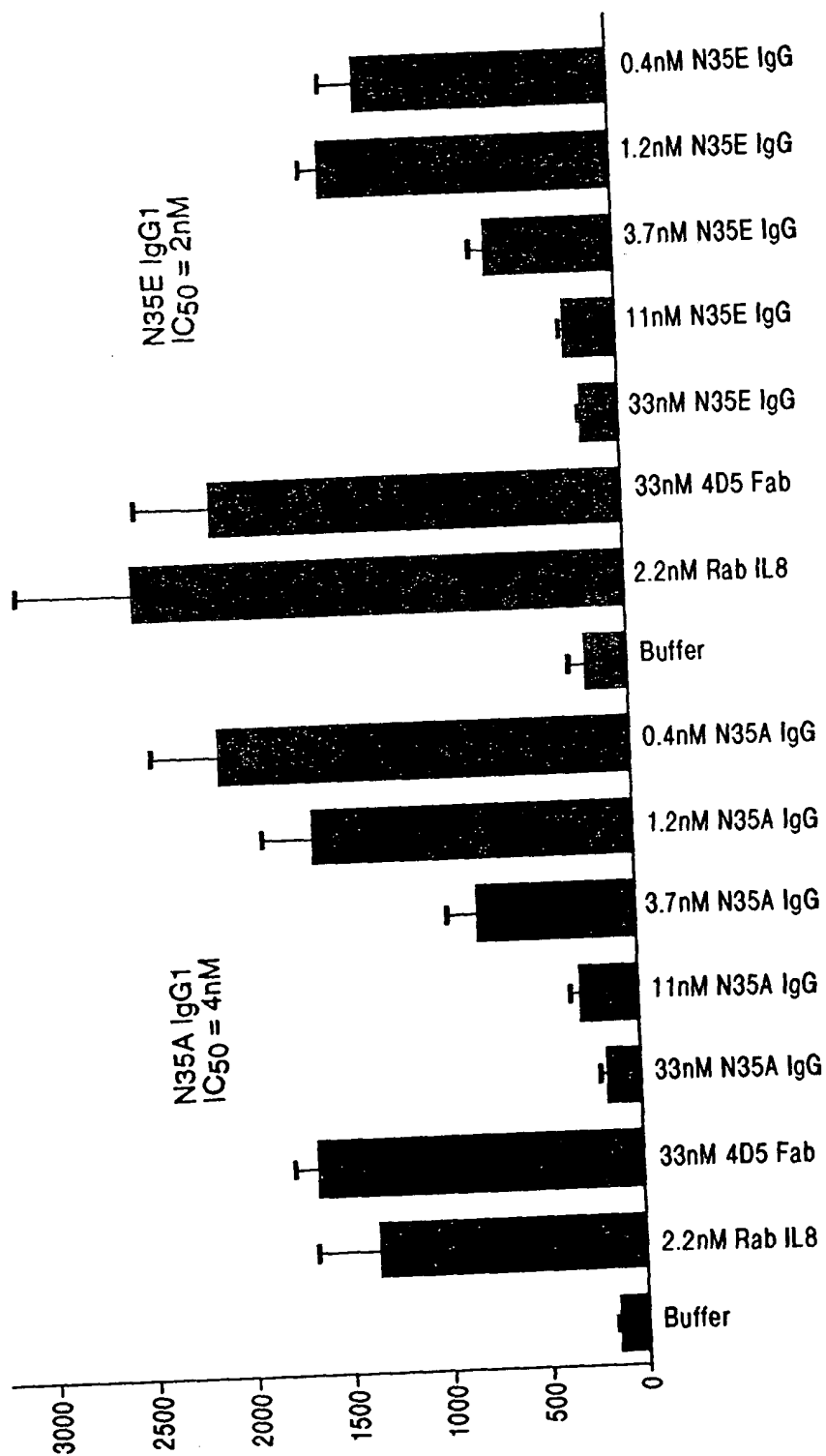


FIG. 50B

Dat T_l/T_s	Dat V_l/V_s
0	250
1000	300
2000	350
3000	400
4000	450
5000	500
6000	550
7000	600
8000	650

Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V1N35A.IgG1

SAMPLE	ka	kd	Kd
Murine 6G4.2.5 IgG2a	8.3×10^5	2.9×10^{-4}	350pM
6G4V11N35A-IgG1	8.7×10^5	7.7×10^{-5}	88pM
6G4V11N35E-IgG1	3.0×10^6	1.4×10^{-4}	49pM

FIG. 51

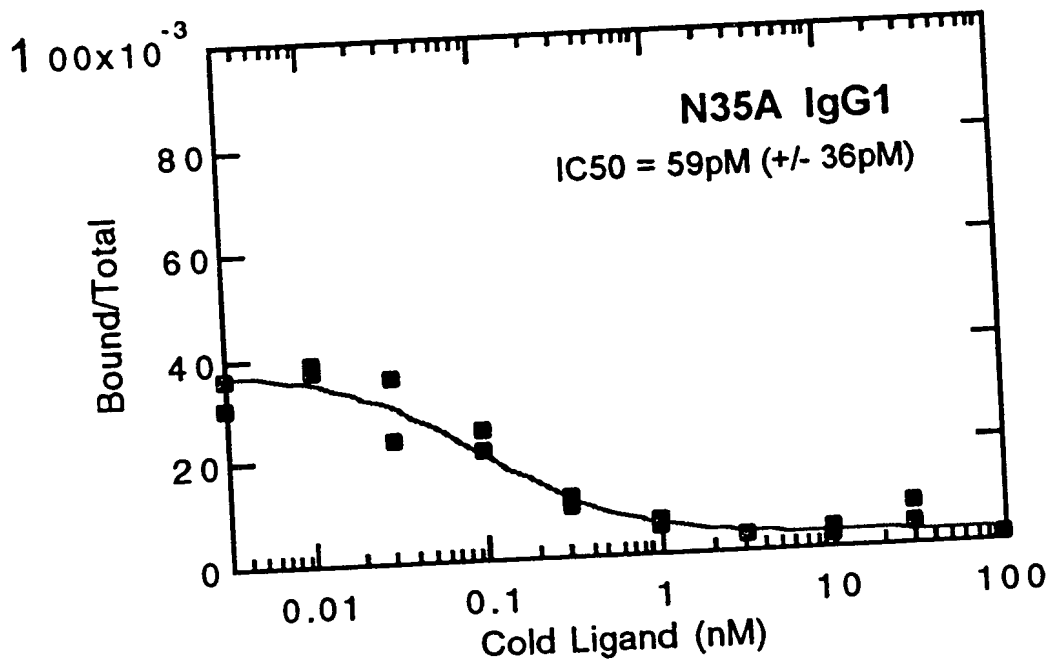


FIG. 52A

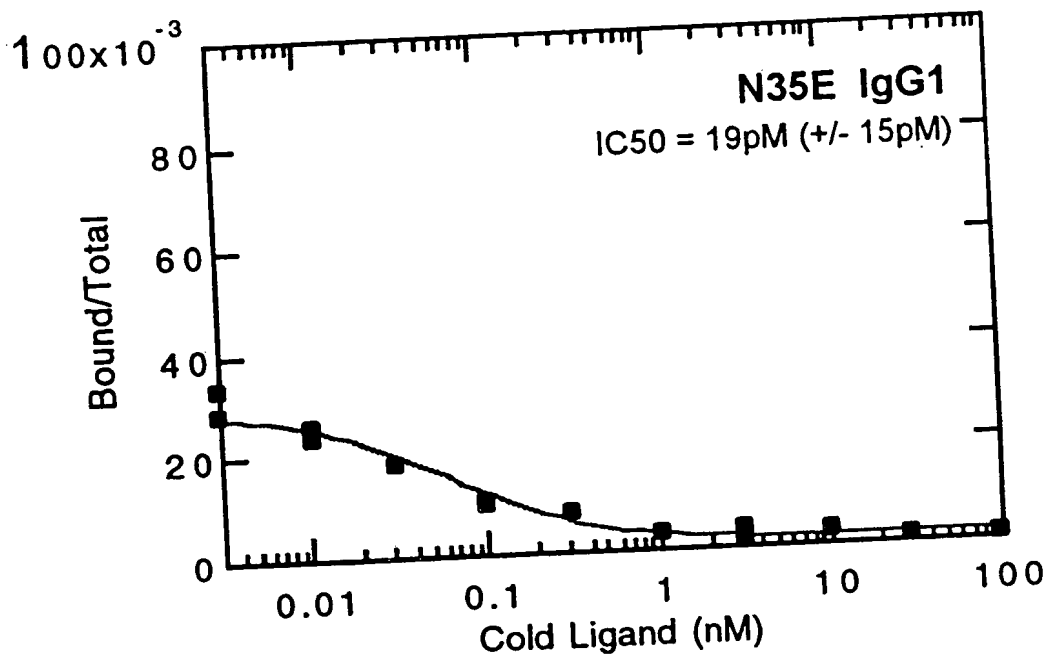


FIG. 52B

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
 TTTTCCCATG GATCTCCAAC TCCACTAAAA TACTTTTTCT TATAGCGTAA AGAAGAACGT
 -1 M K K N I A F L L A

841 TCTATGTTCTG TTTTCTCTAT TGCTACAAAC GCGTACGCTG AGGTTCAGCT AGTGCAGTCT
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
 -11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
 CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
 8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
 48 V G Y I D P S N G E T T Y N Q K F K G R

1081 TTCACCTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
 68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTAAGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCTTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
 AAGAAGCTGC AGACCCCACT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
 108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGGTG TCGCCGGGAC
 128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
 CCGACGGACC AGTTCTGTAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
 148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCCGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
 GACTGGTTCG CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L

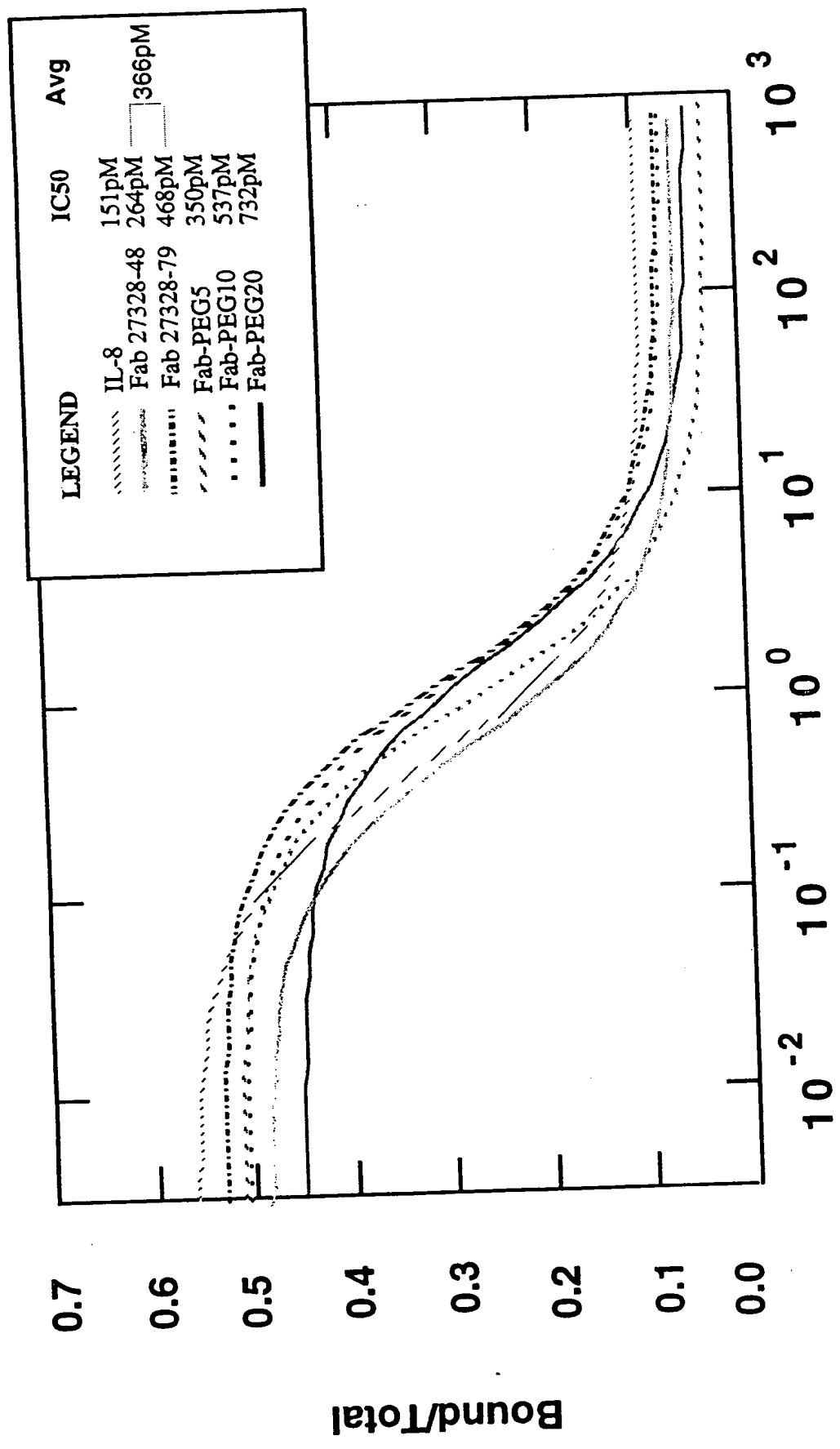
1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
 TCGTCGCACC ACTGGCACGG GAGGTGCTCG AACCCTGGG TCTGGATGTA GACGTTGCAC
 188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
 TTAGTGTTCTG GGTCTGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
 208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCGCGCCGTGA (SEQ ID NO.69)
 TGAGTGTGTA CGGGCGGCACT
 228 T H T C P P O (SEQ ID NO.70)

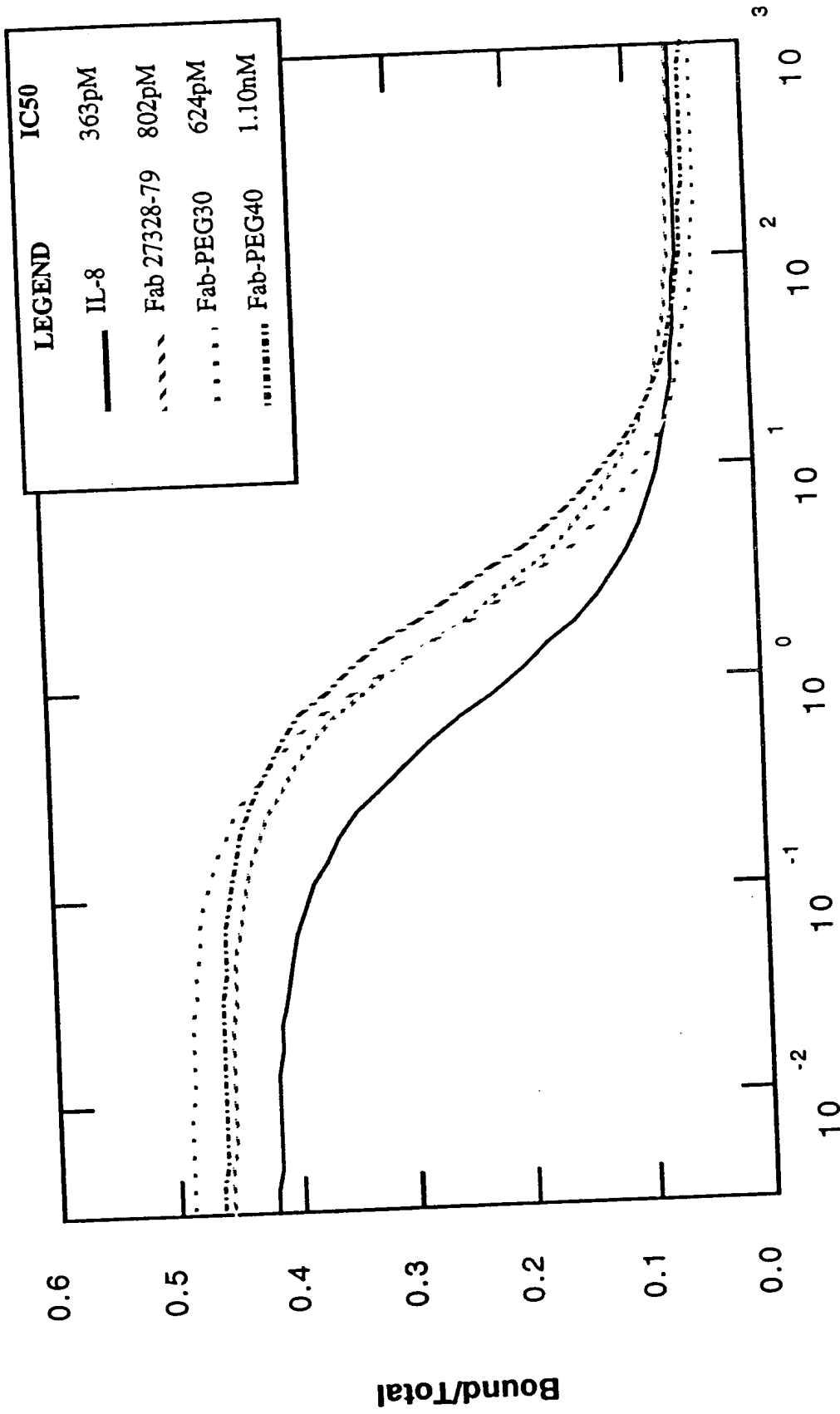
FIG. 53

REF ID: A66666



Antibody Competitor (nM)
 FIG. 54A

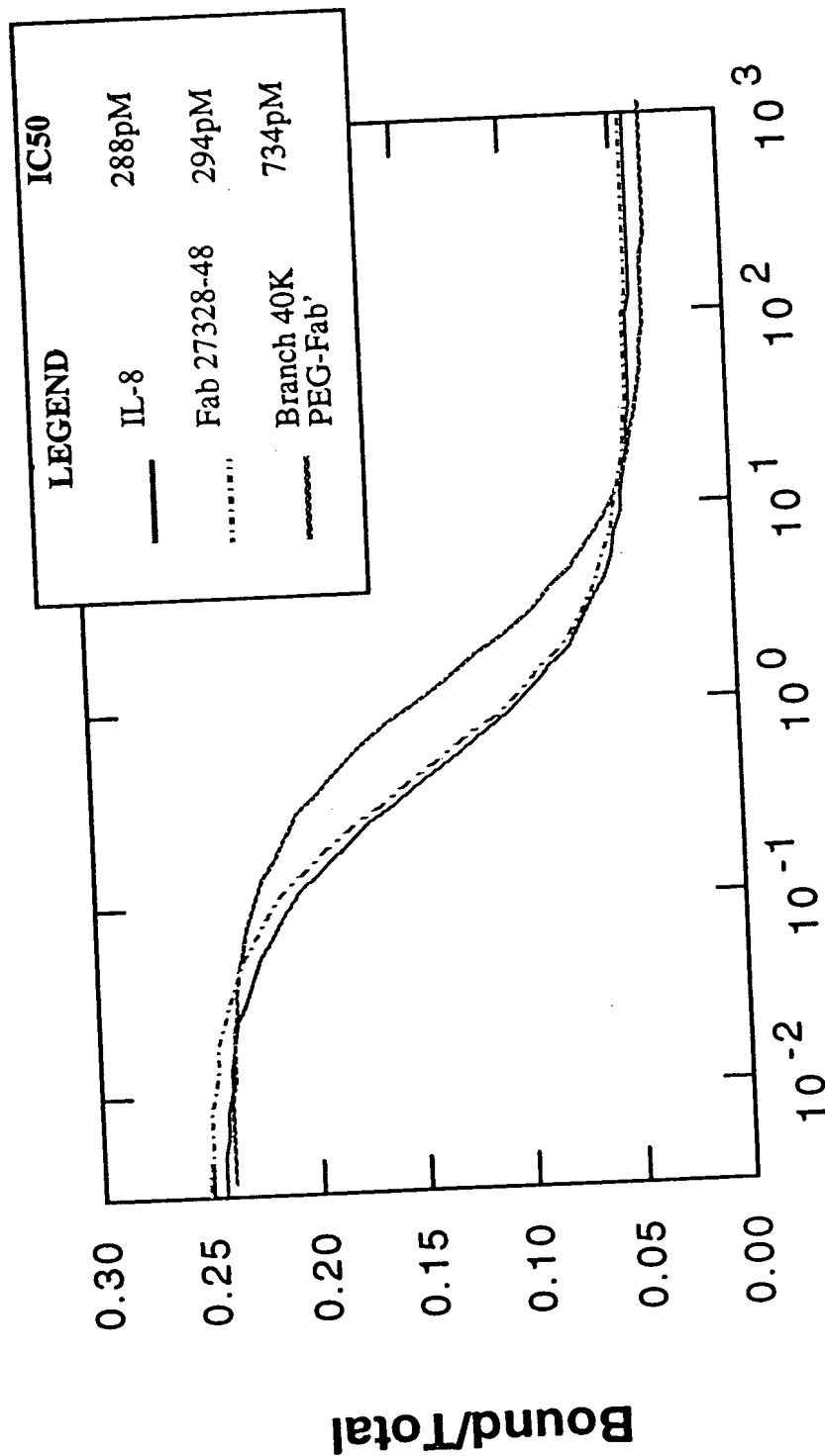
FIG. 54B



Antibody Competitor (nM)

FIG. 54B

FIG. 54C



Antibody Competitor (nM)

FIG. 54C

2000-03-22

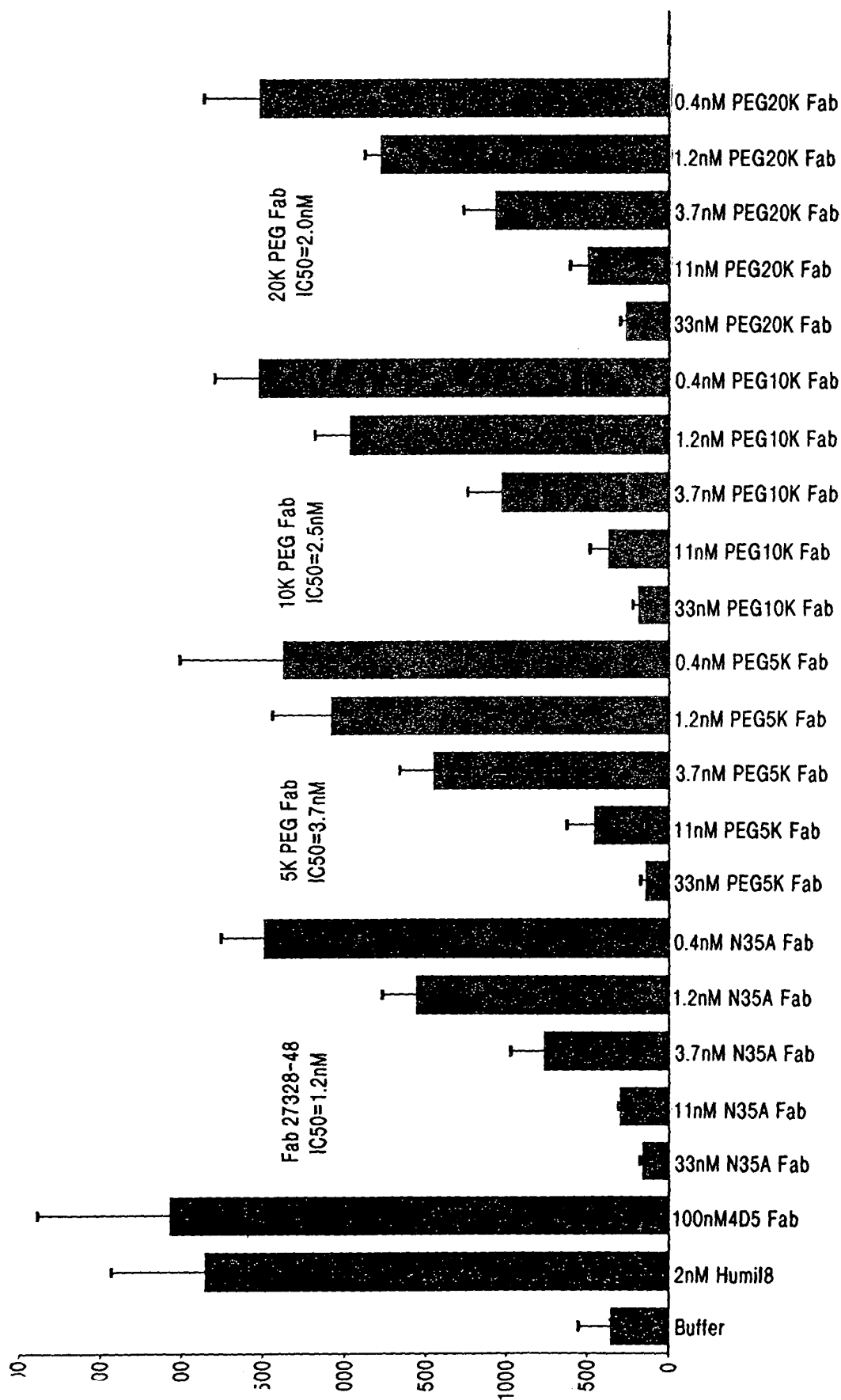


FIG. 55A

FIG. 55B

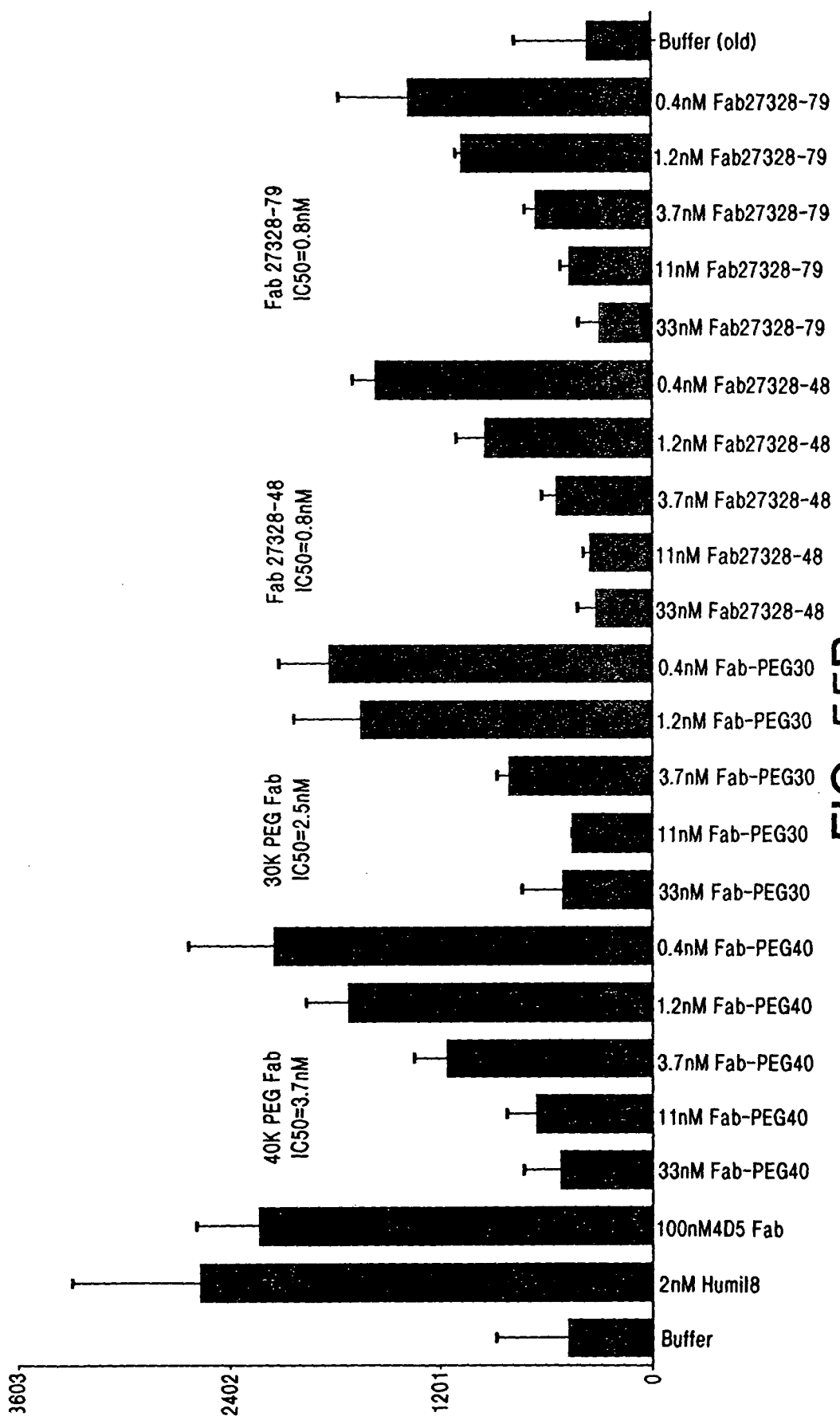


FIG. 55B

FIG. 55C

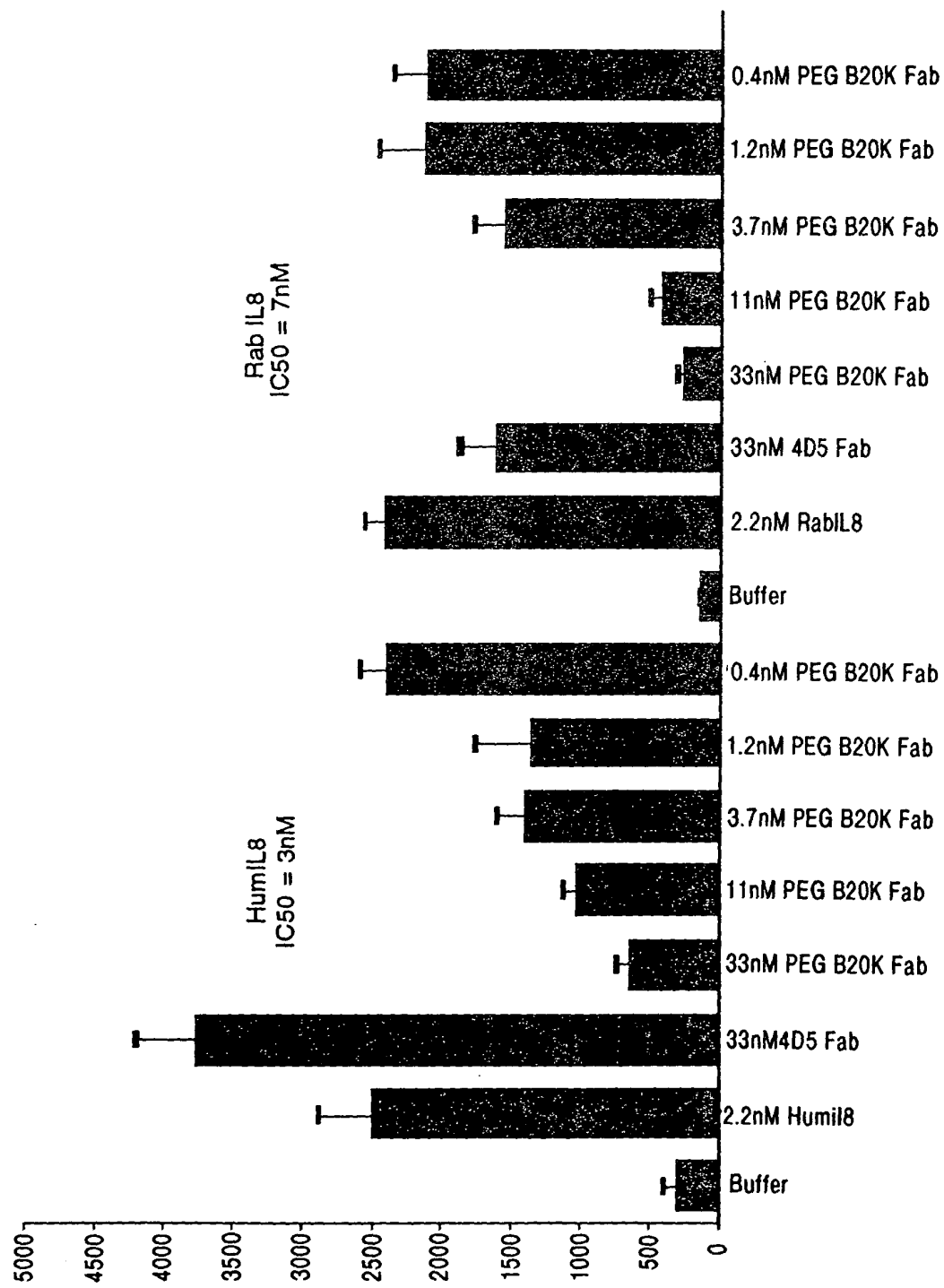
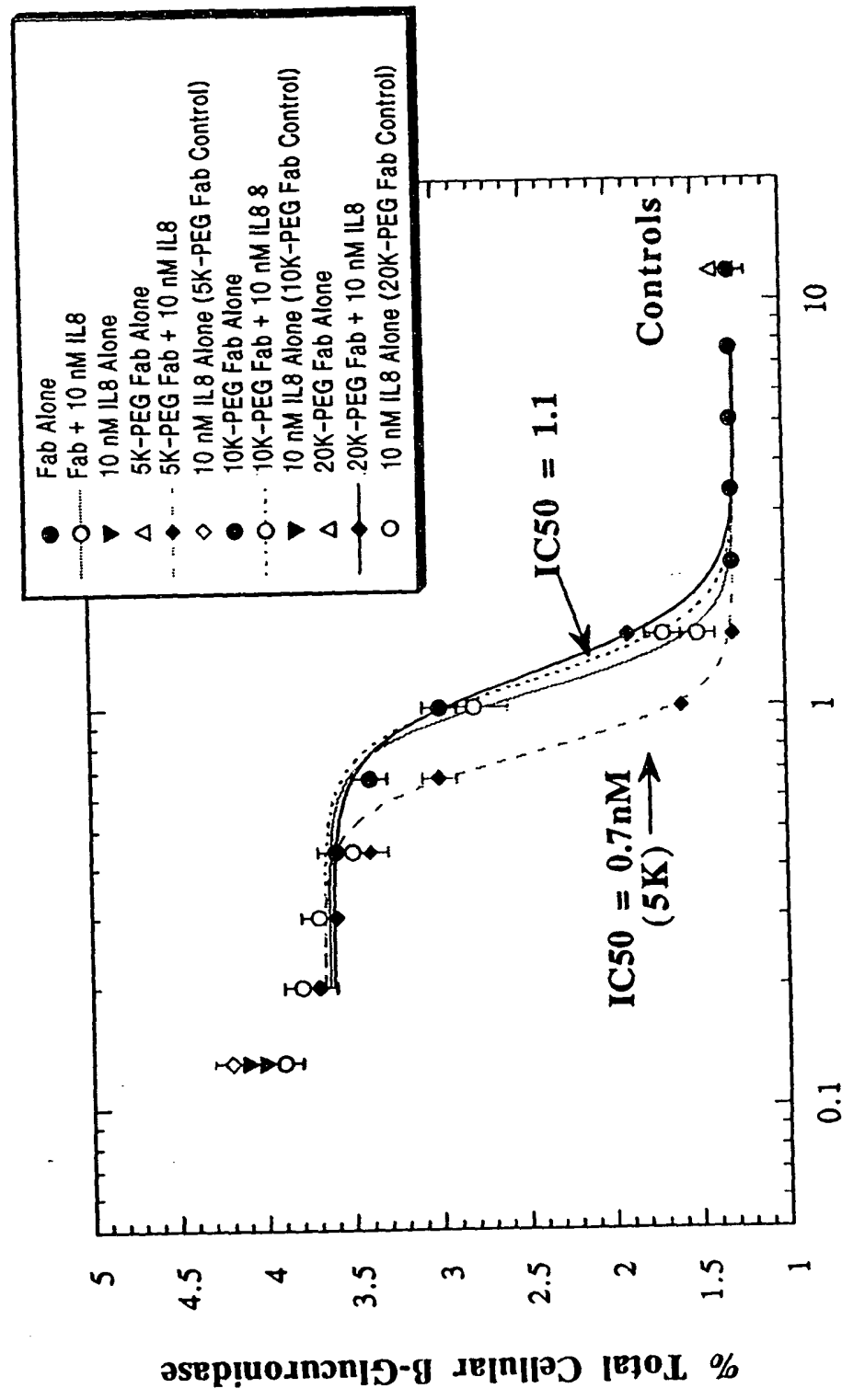


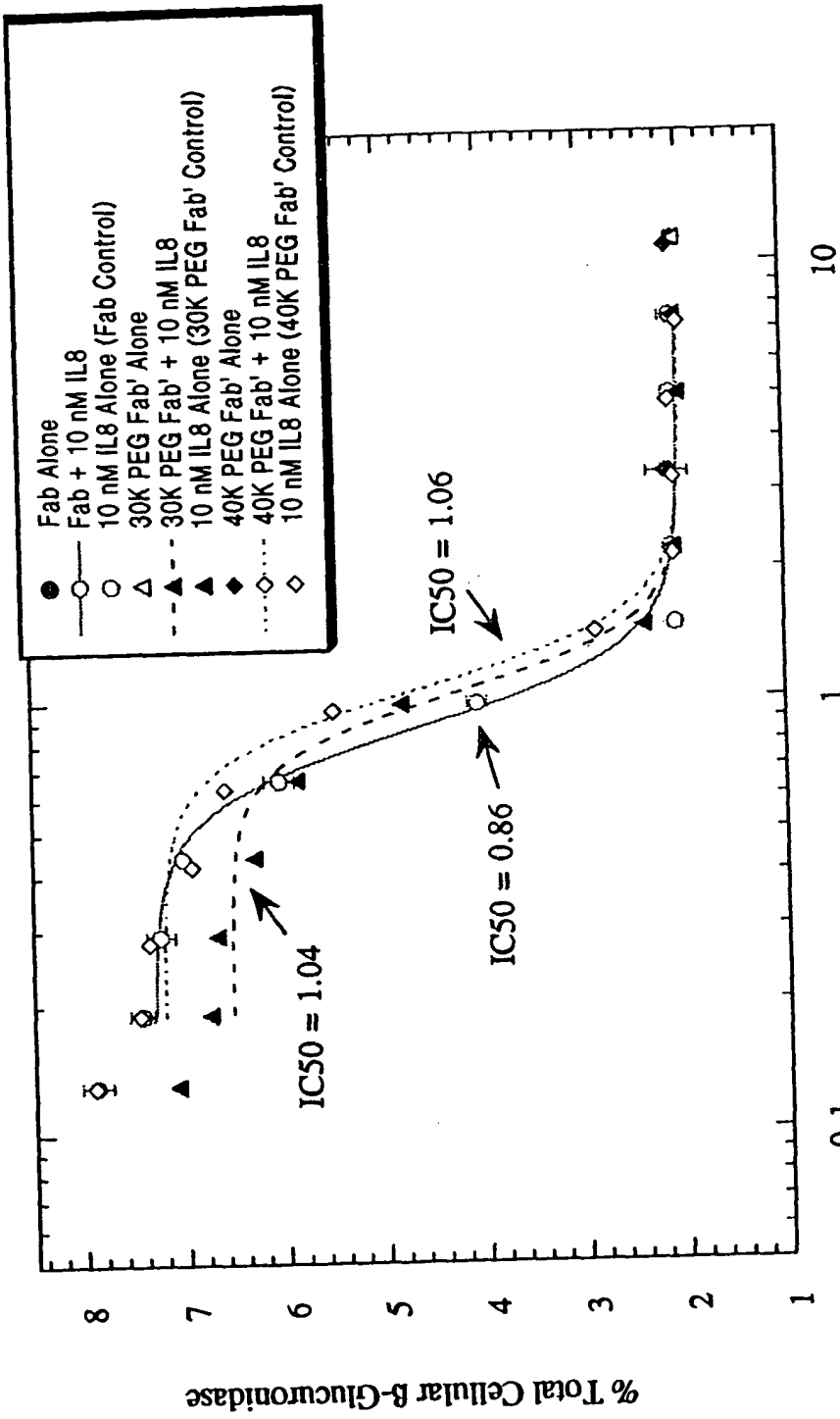
FIG. 55C

TOP SECRET 33268



Molar Ratio Antibody:IL-8

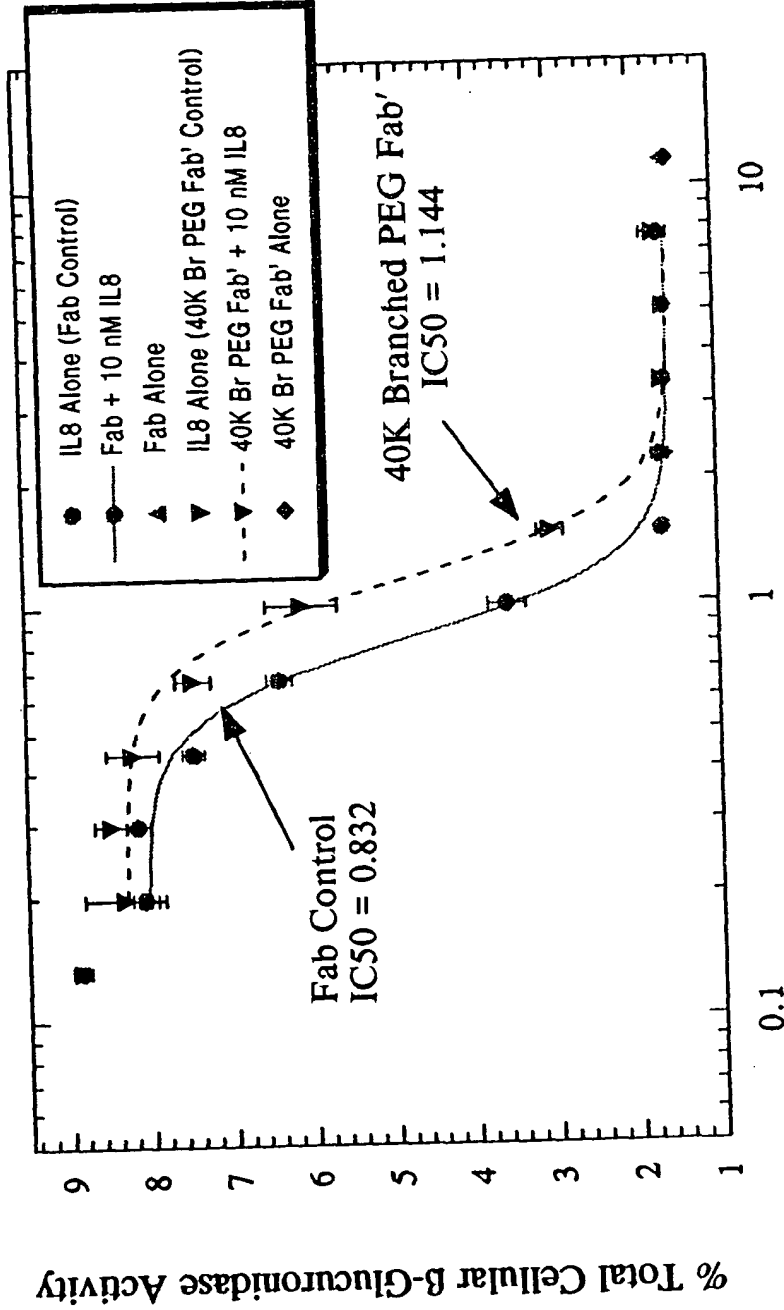
FIG. 56A



Molar Ratio Antibody:IL-8

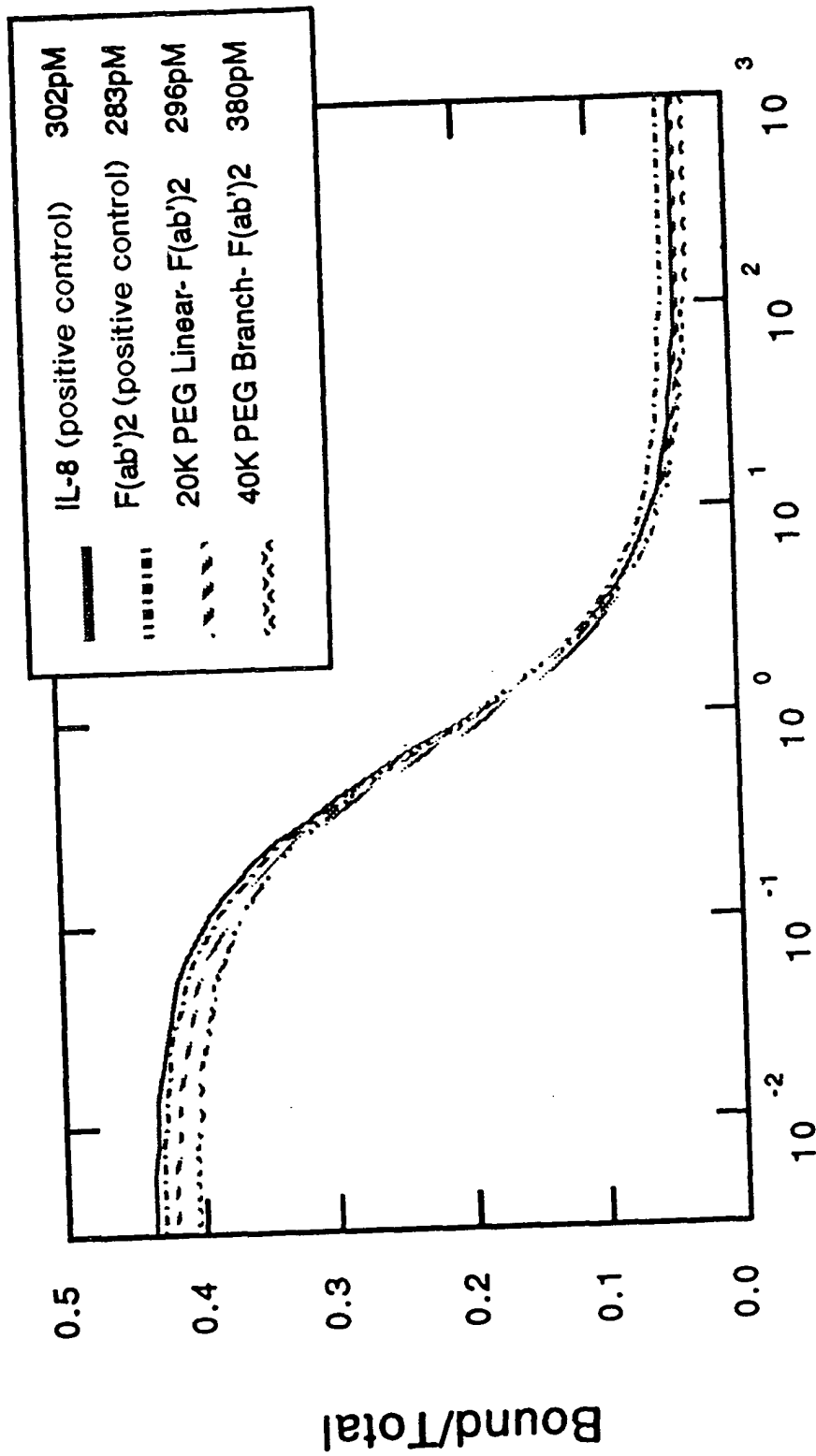
FIG. 56B

TOP SECRET



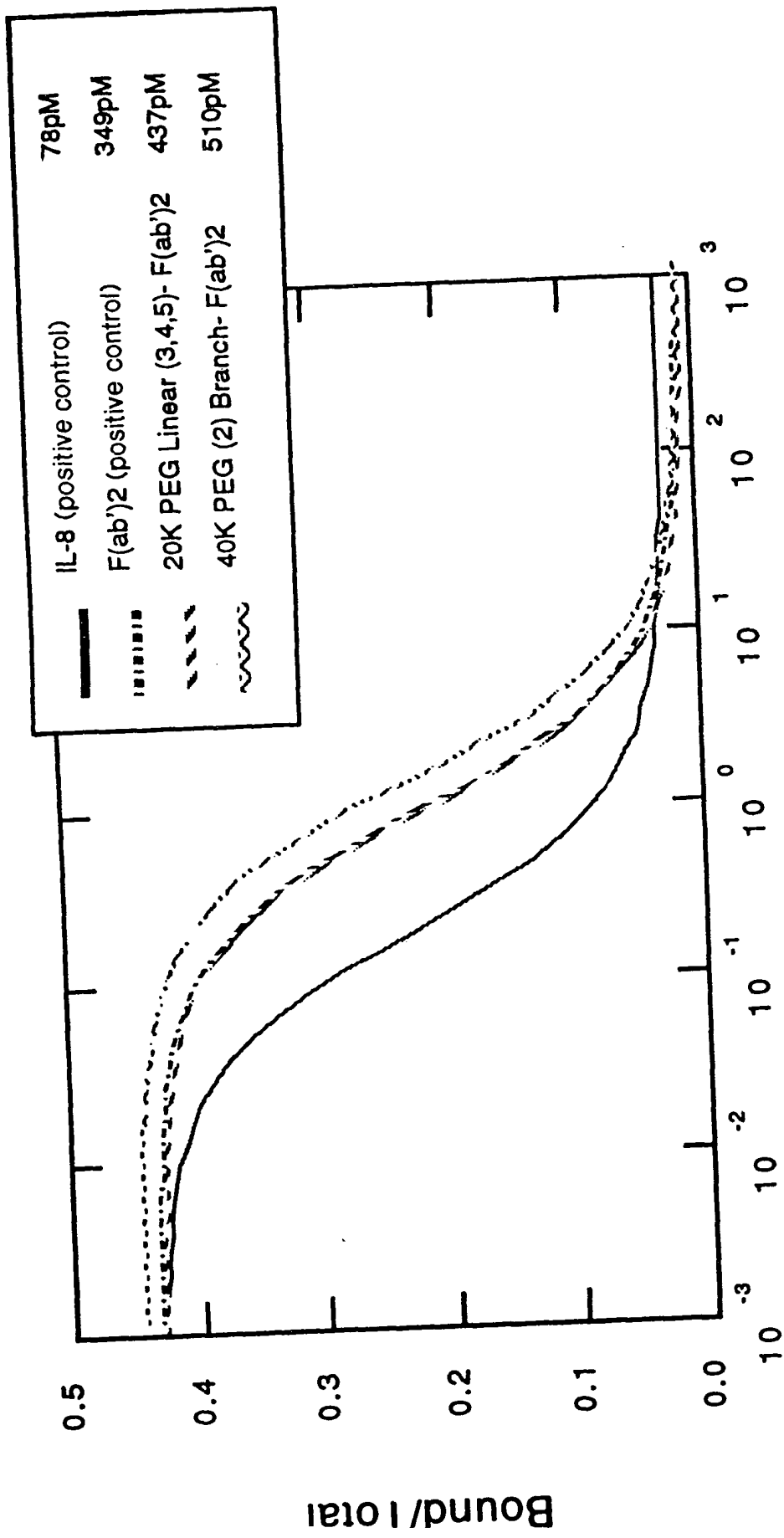
Molar Ratio Antibody:IL8

FIG. 56C



Pegylated F(ab')₂ (nM)

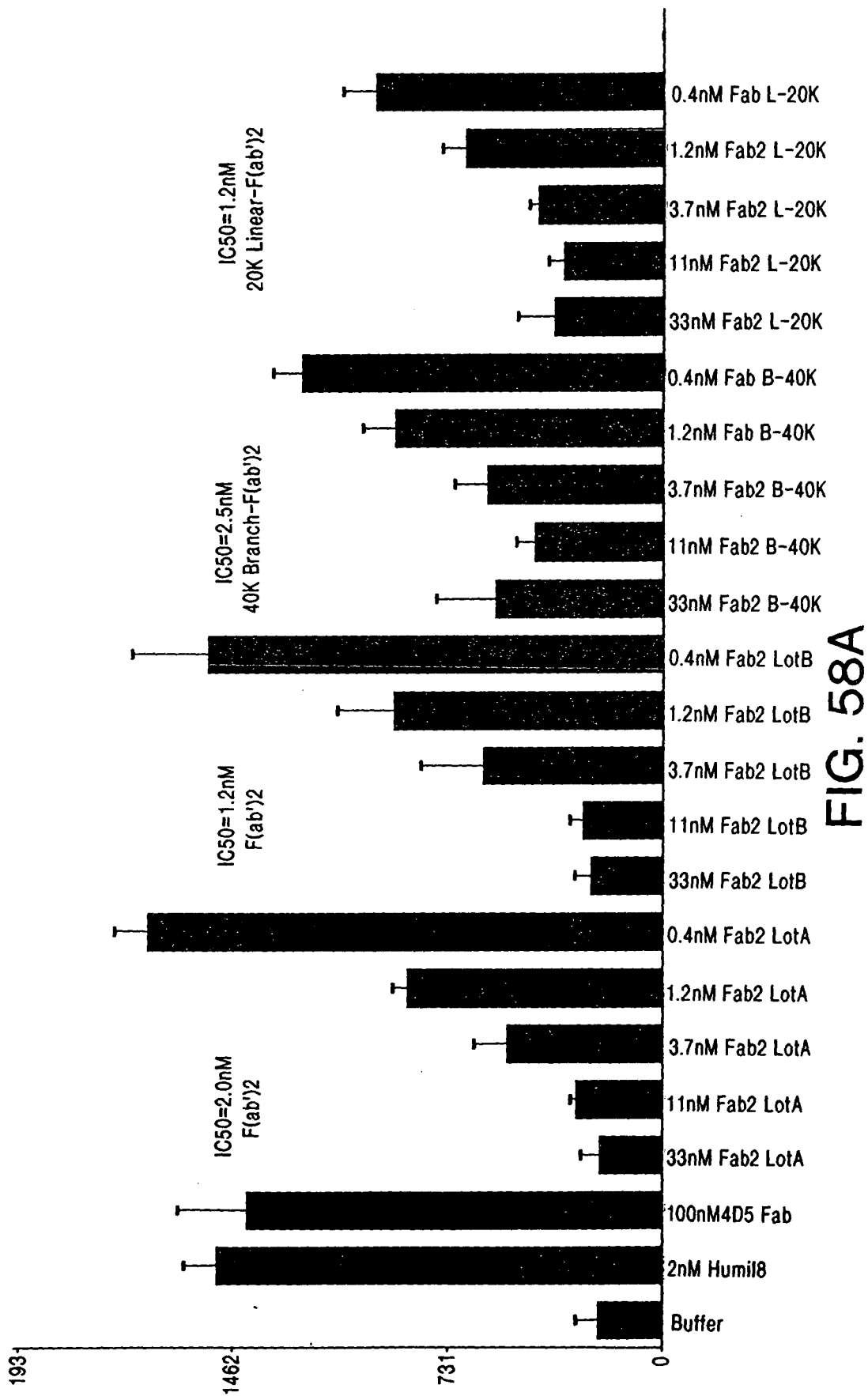
FIG. 57A



Pegylated F(ab')₂ (nM)

FIG. 57B

FIG. 58A



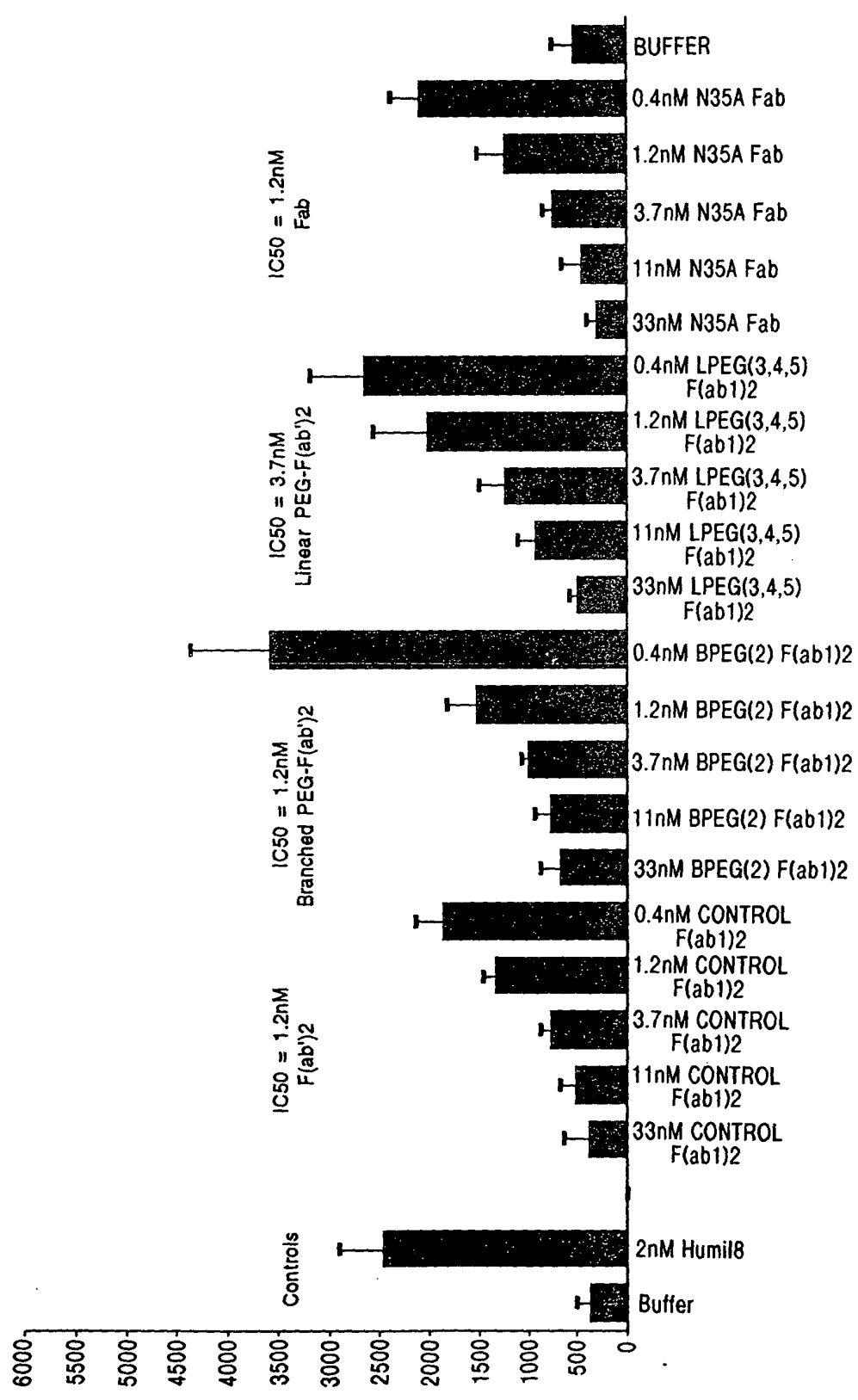
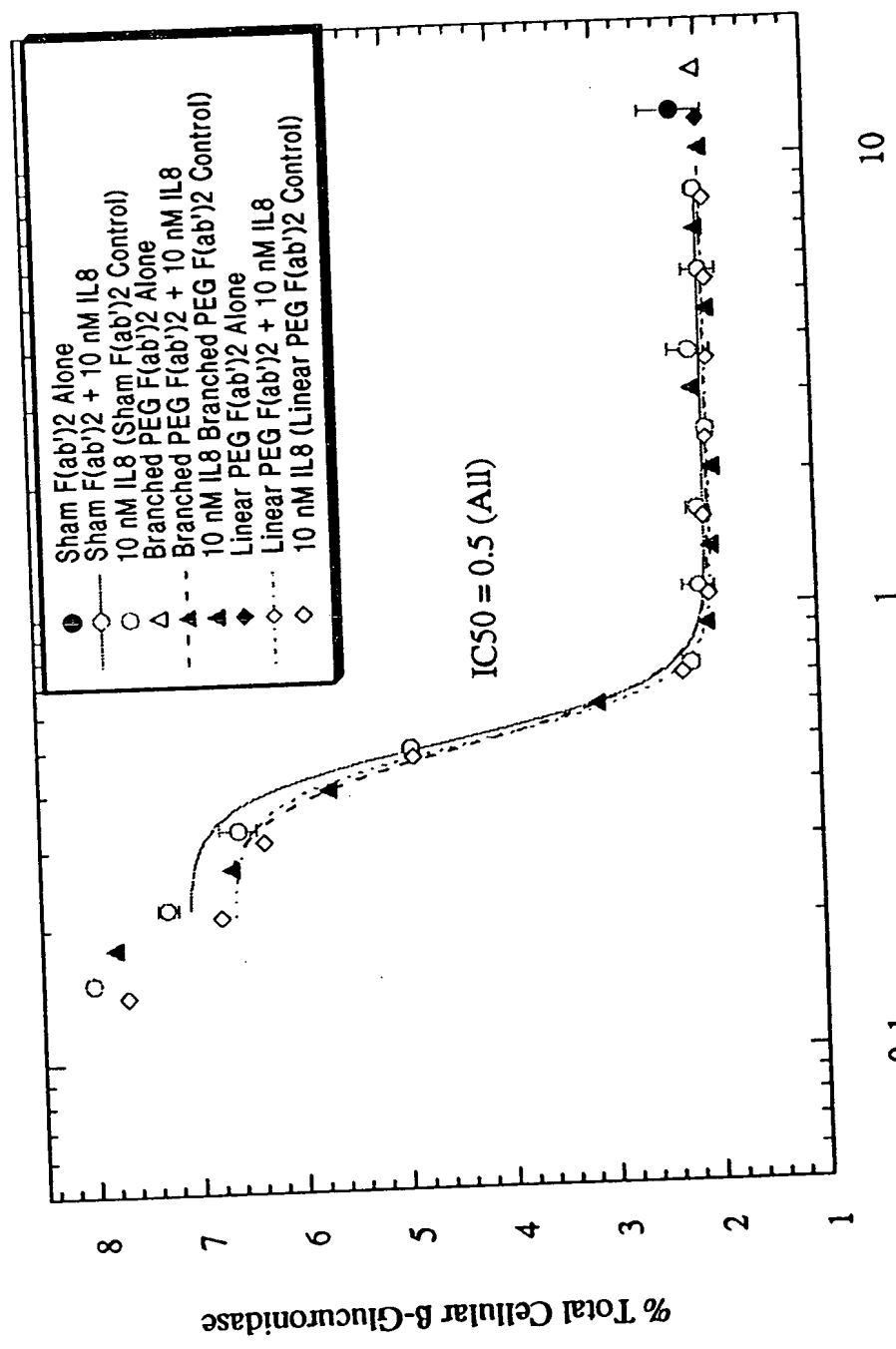


FIG. 58B



Molar Ratio Antibody:IL-8

FIG. 59A

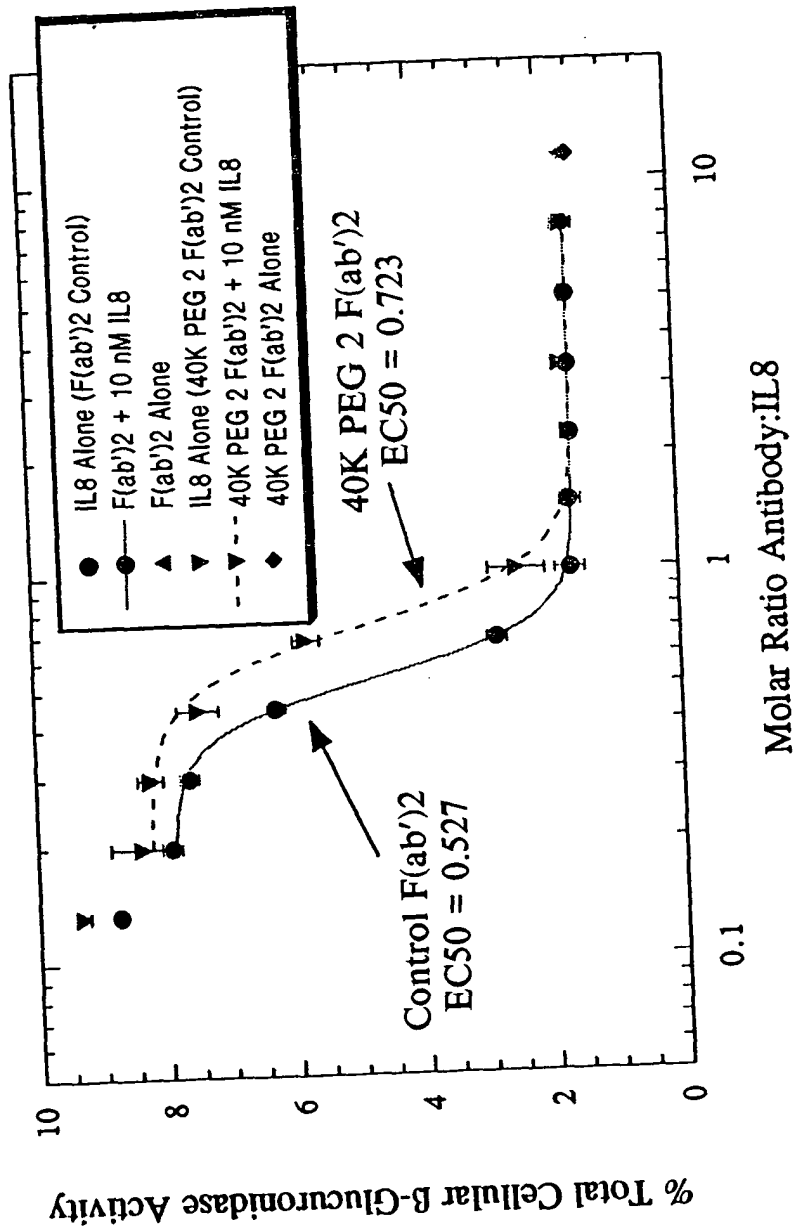


FIG. 59B

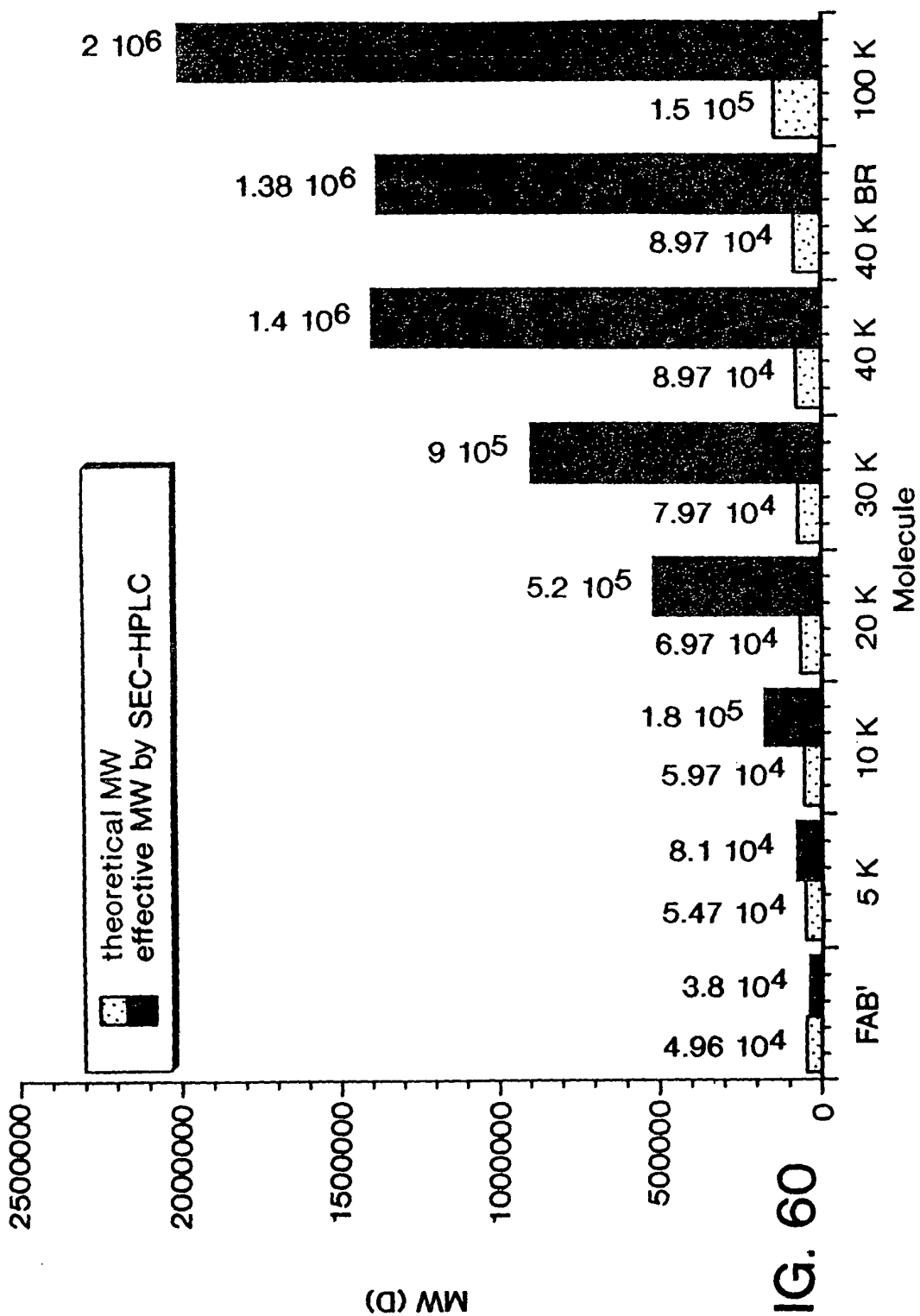


FIG. 60

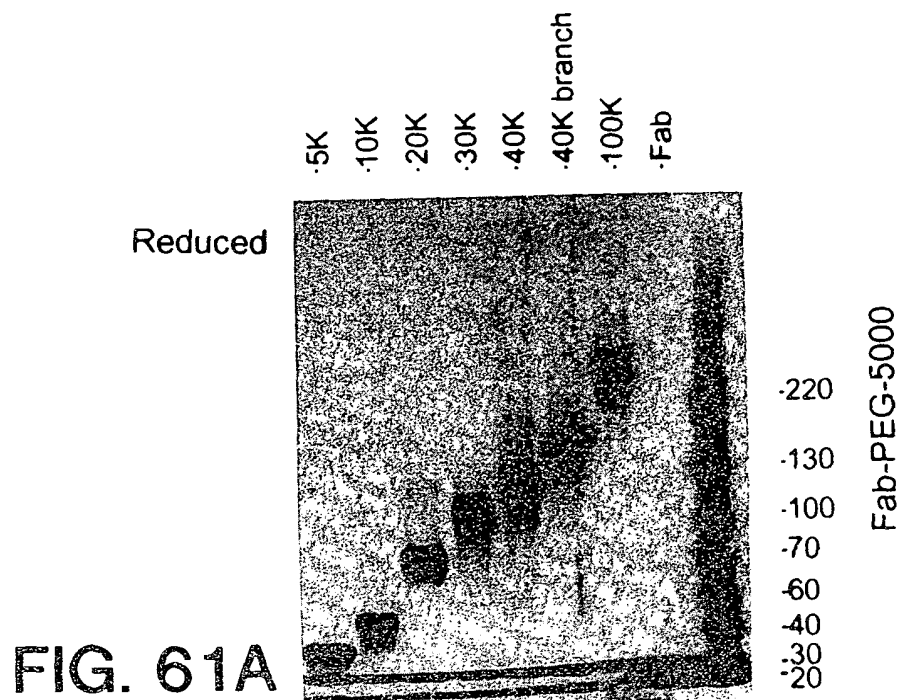


FIG. 61A

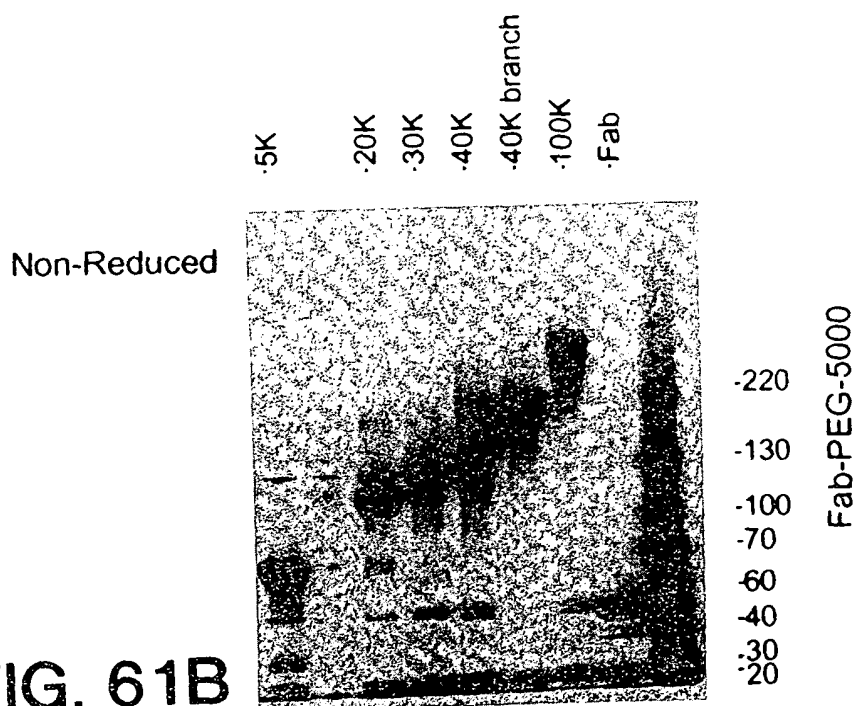


FIG. 61B

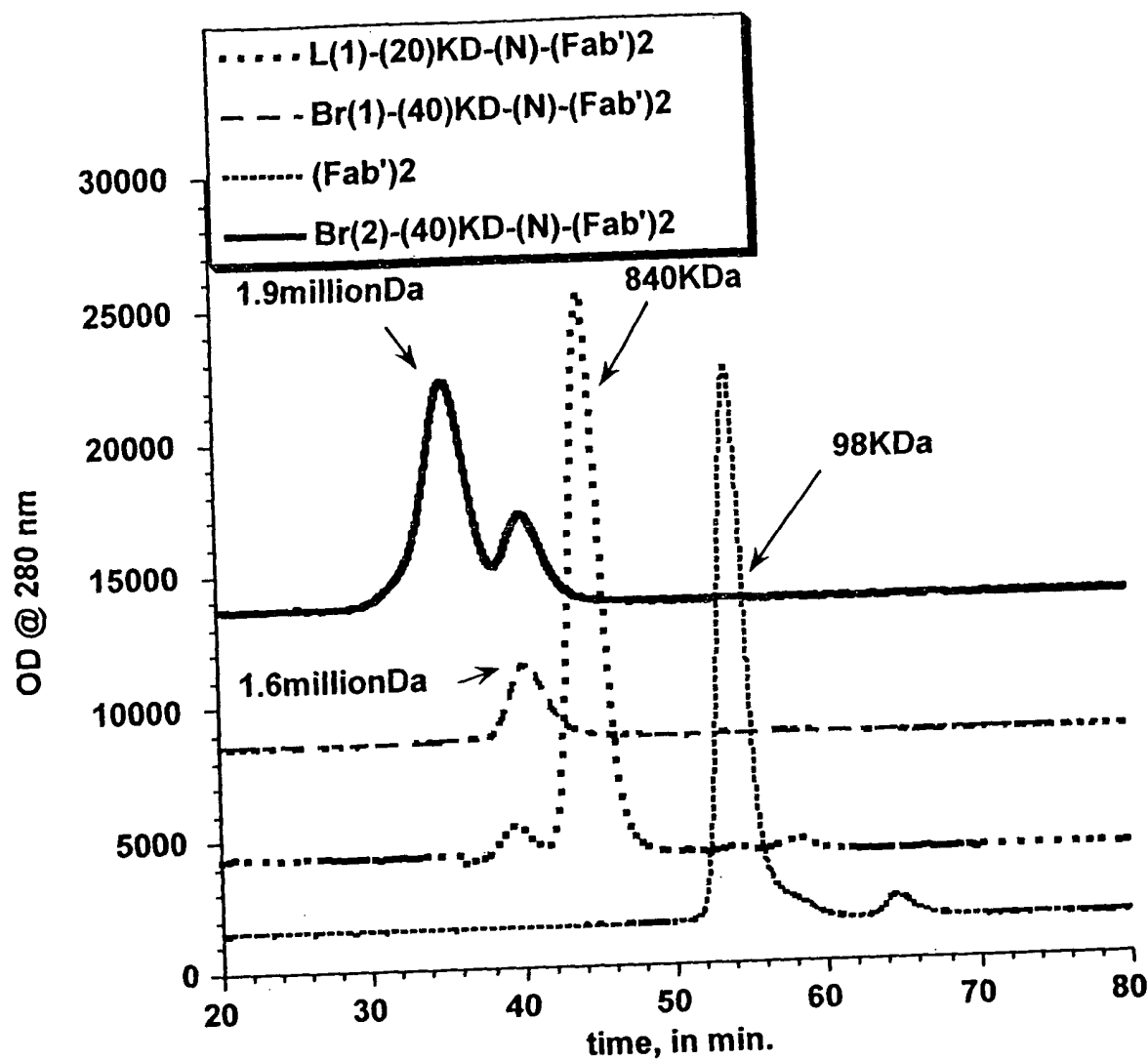


FIG. 62

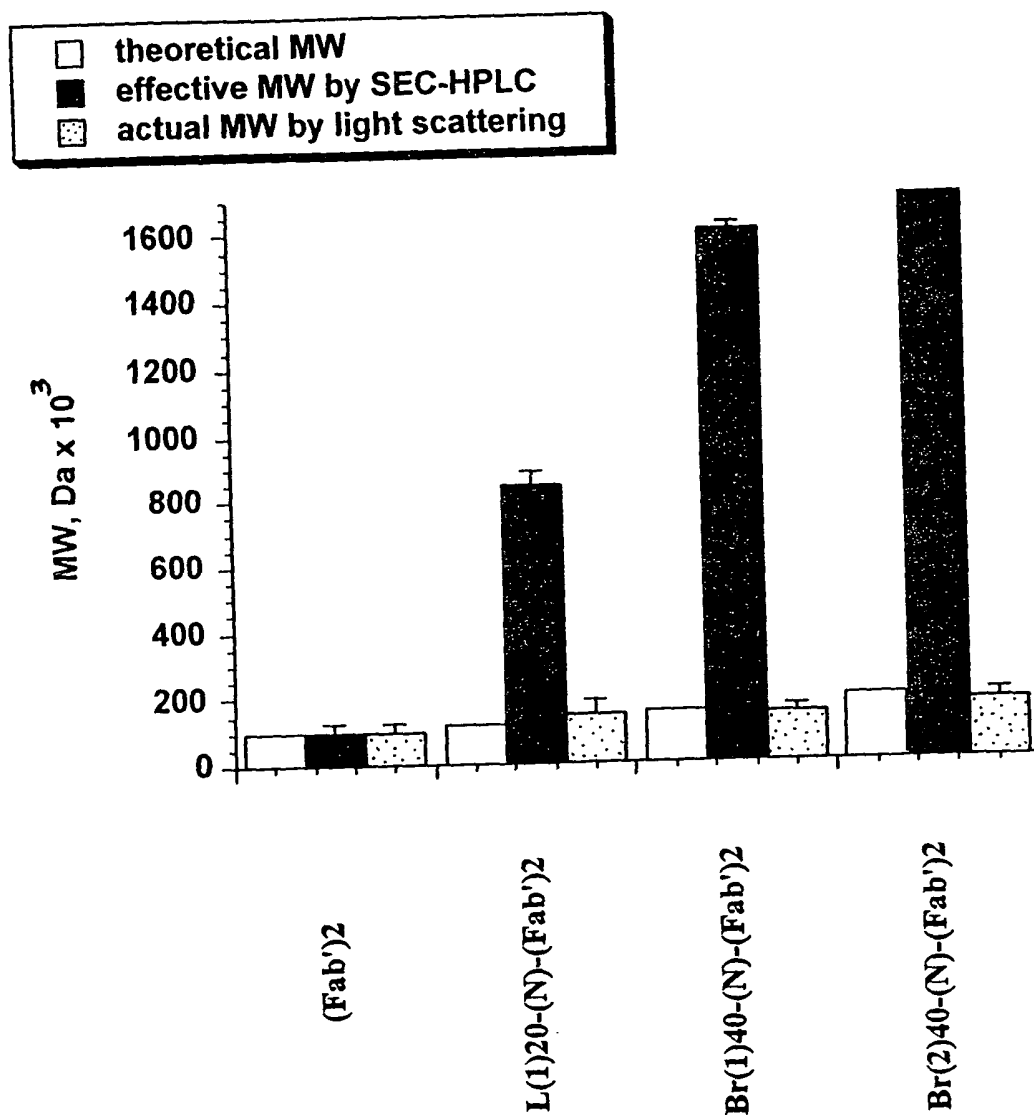


FIG. 63

REF ID: A66926

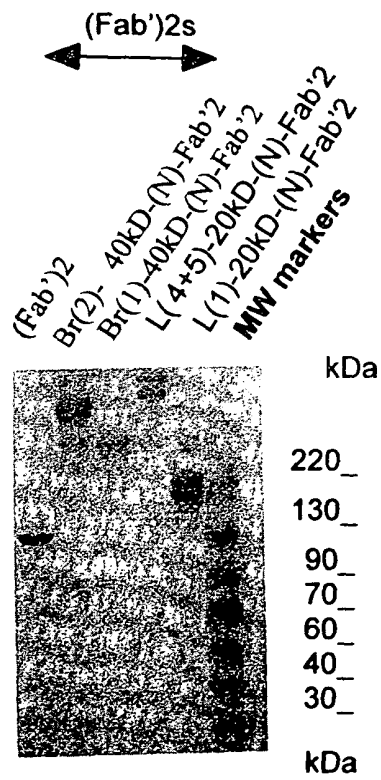
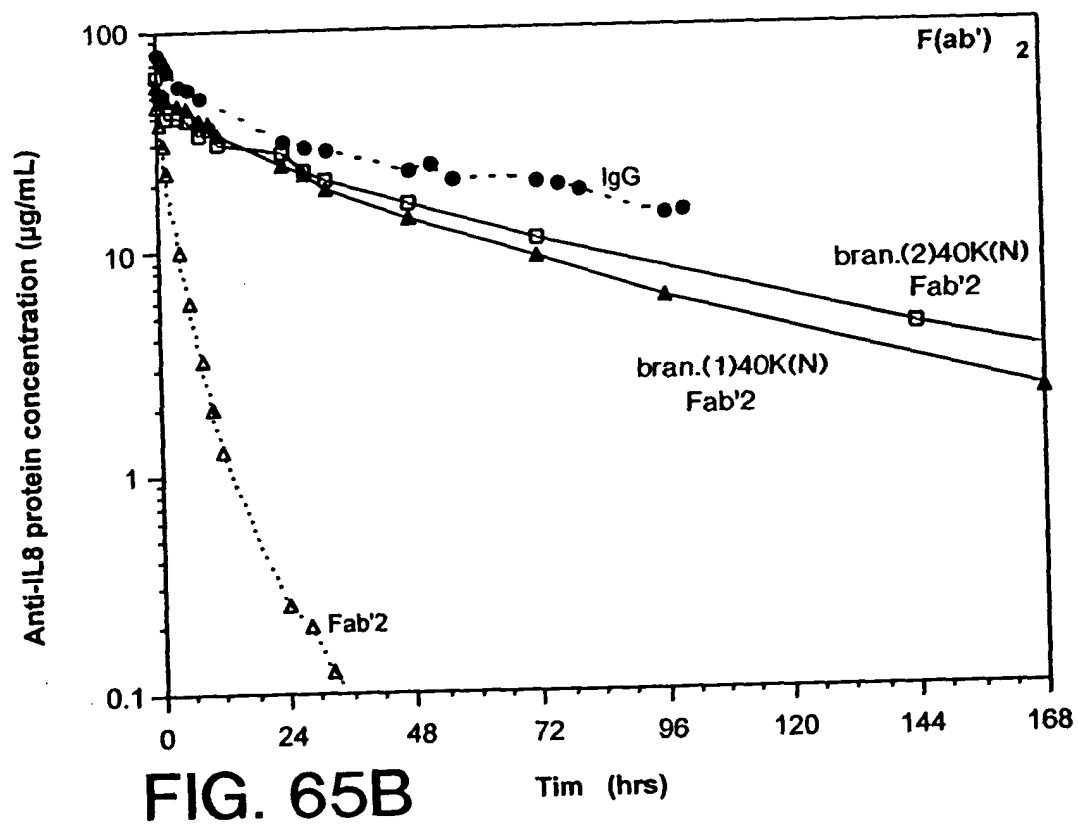
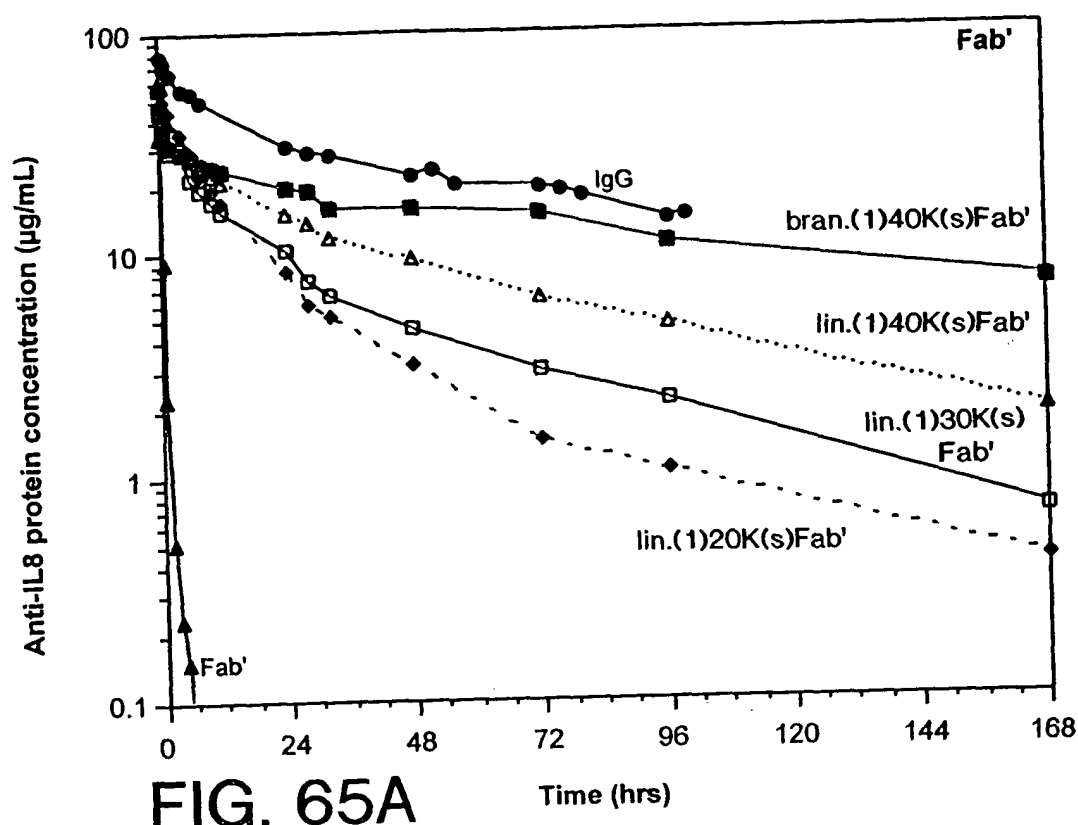


FIG. 64



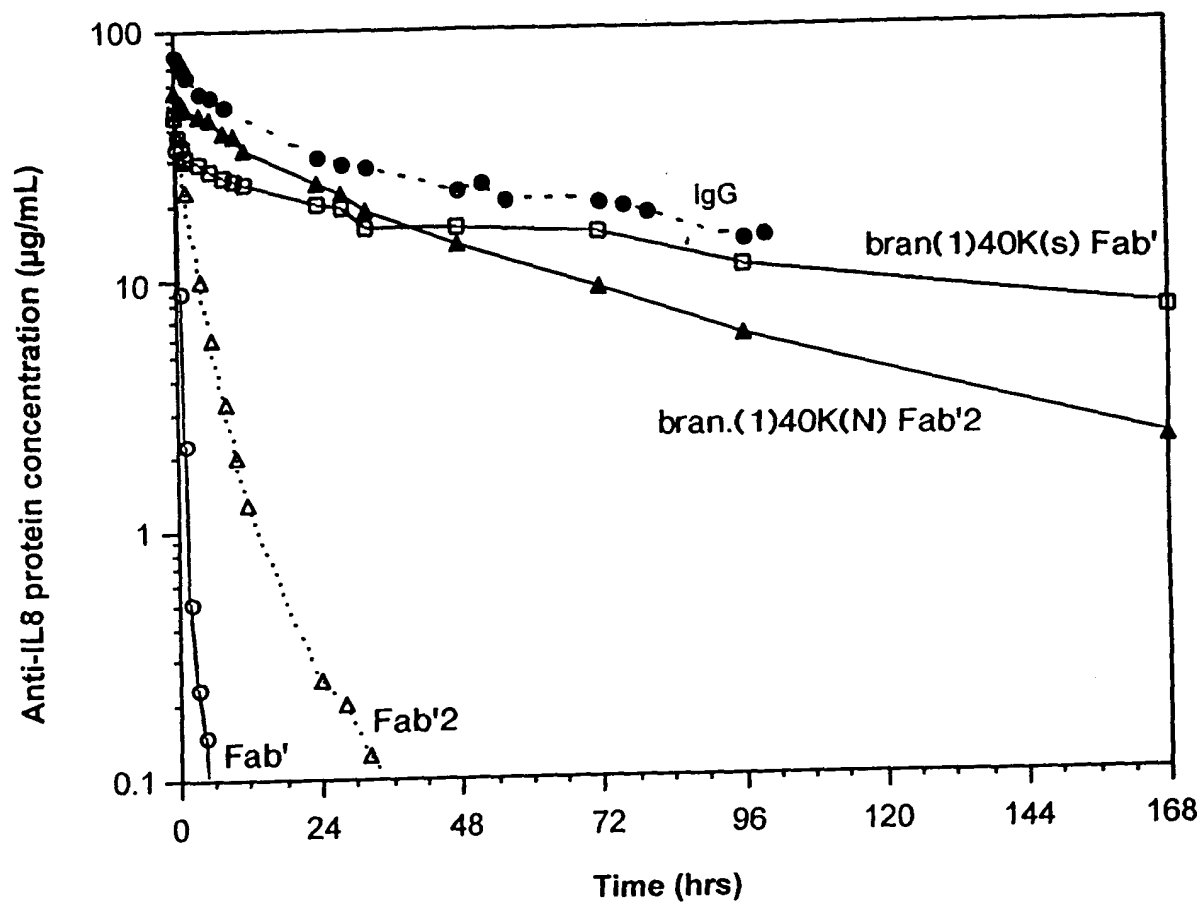


FIG. 66

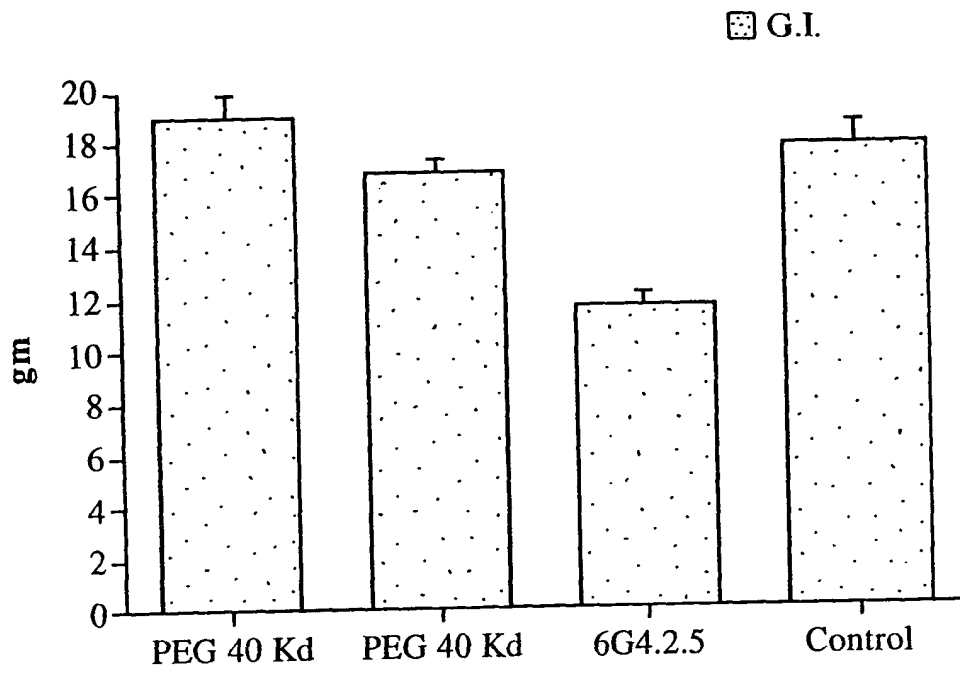


FIG. 67

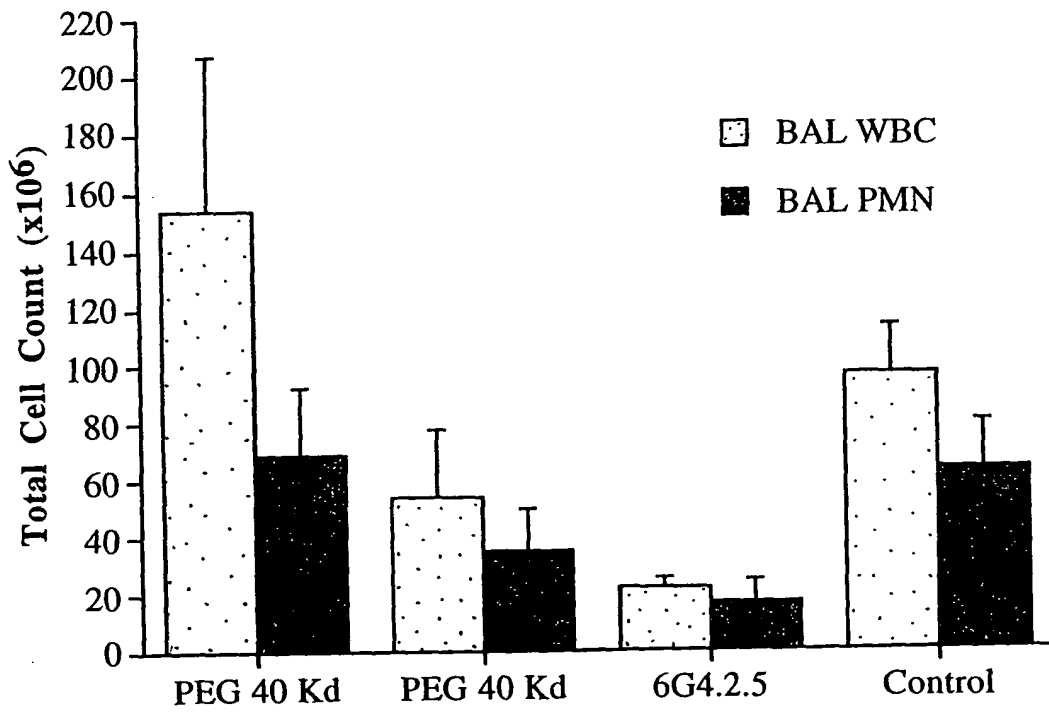


FIG. 68

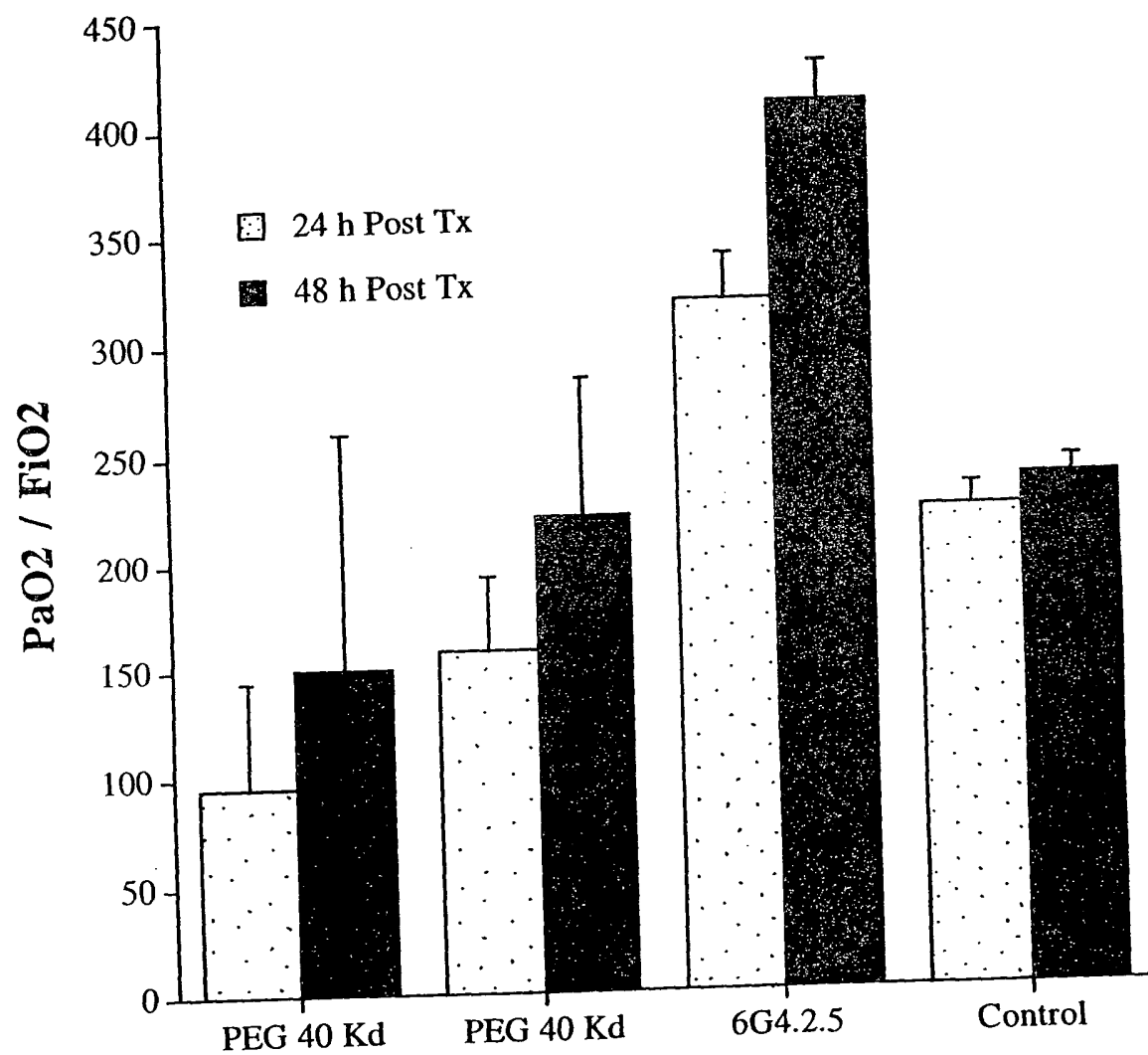


FIG. 69

FIG. 70A

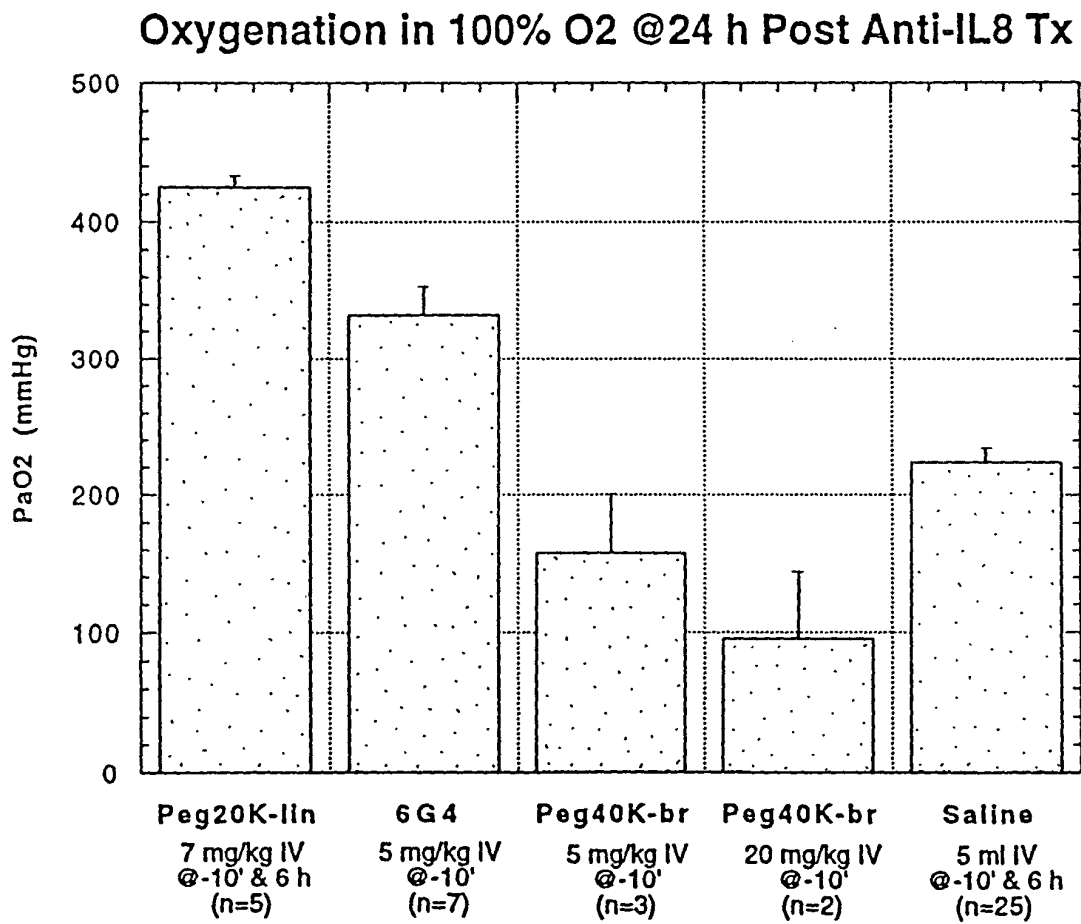


FIG. 70A

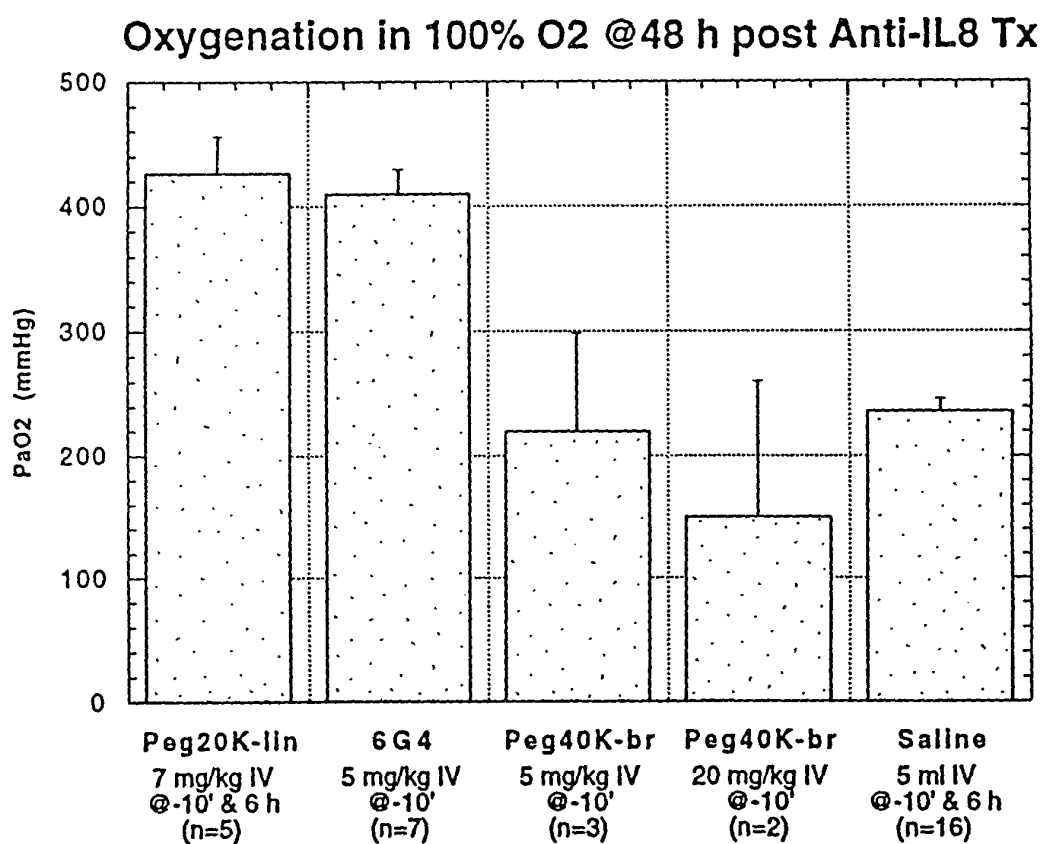


FIG. 70B

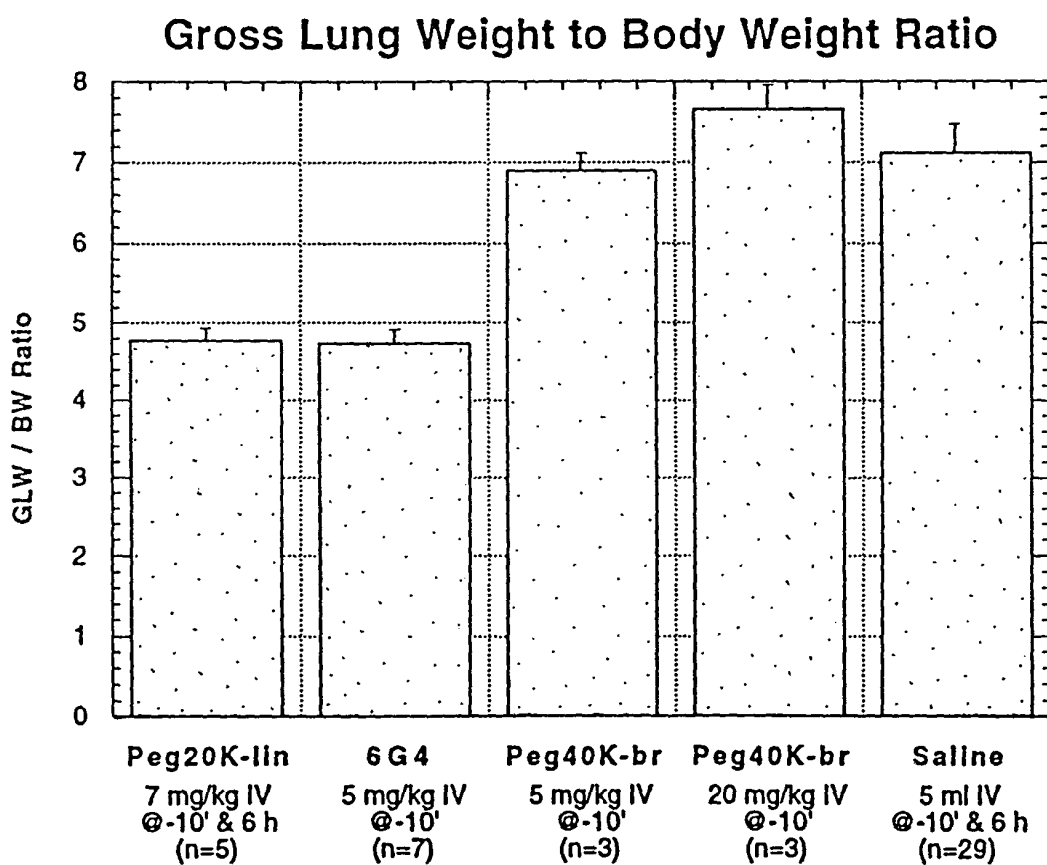


FIG. 70C

FIG. 70D

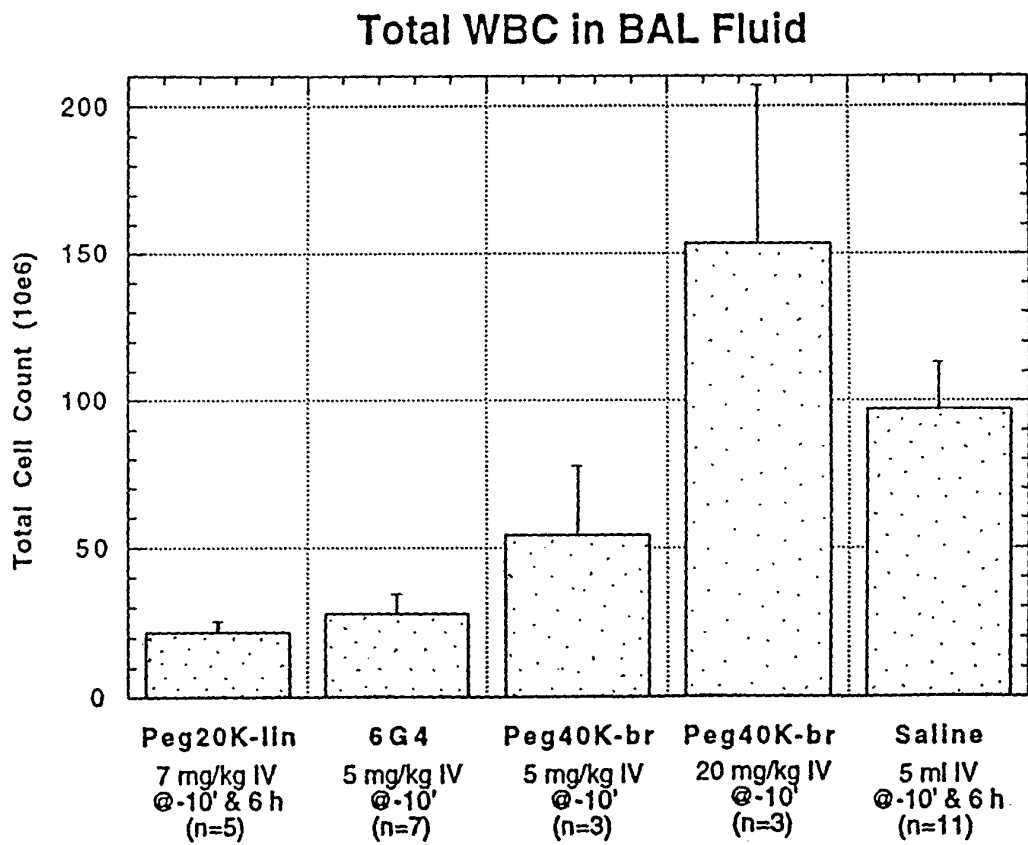


FIG. 70D

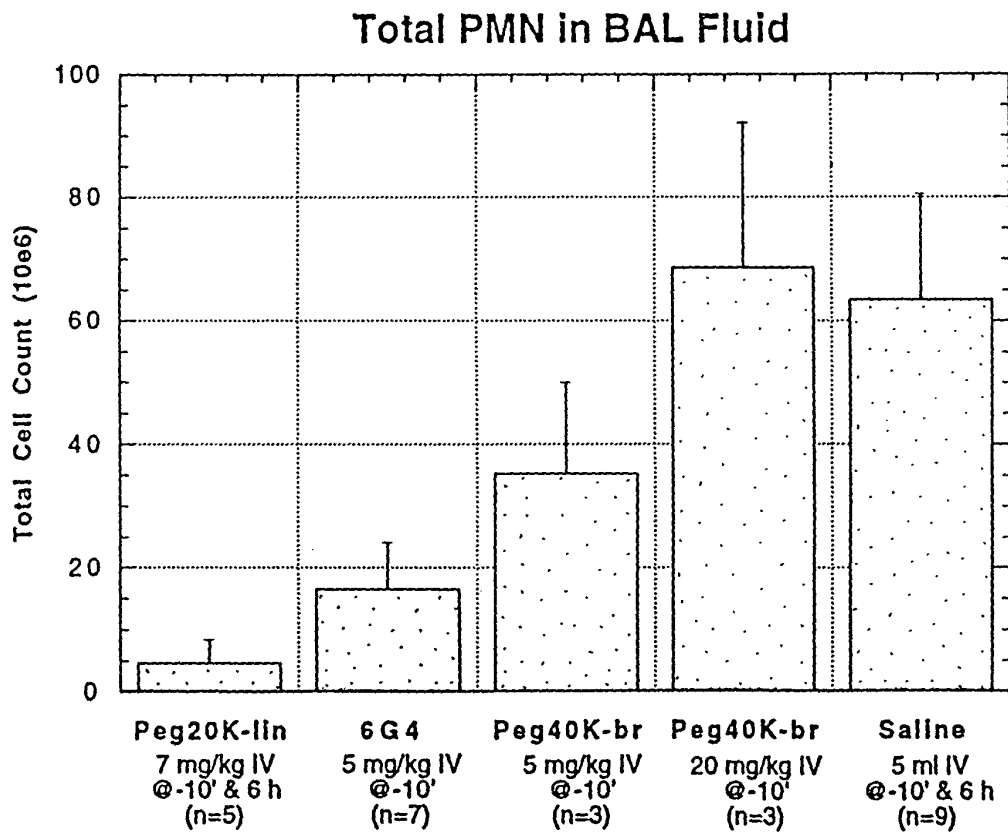
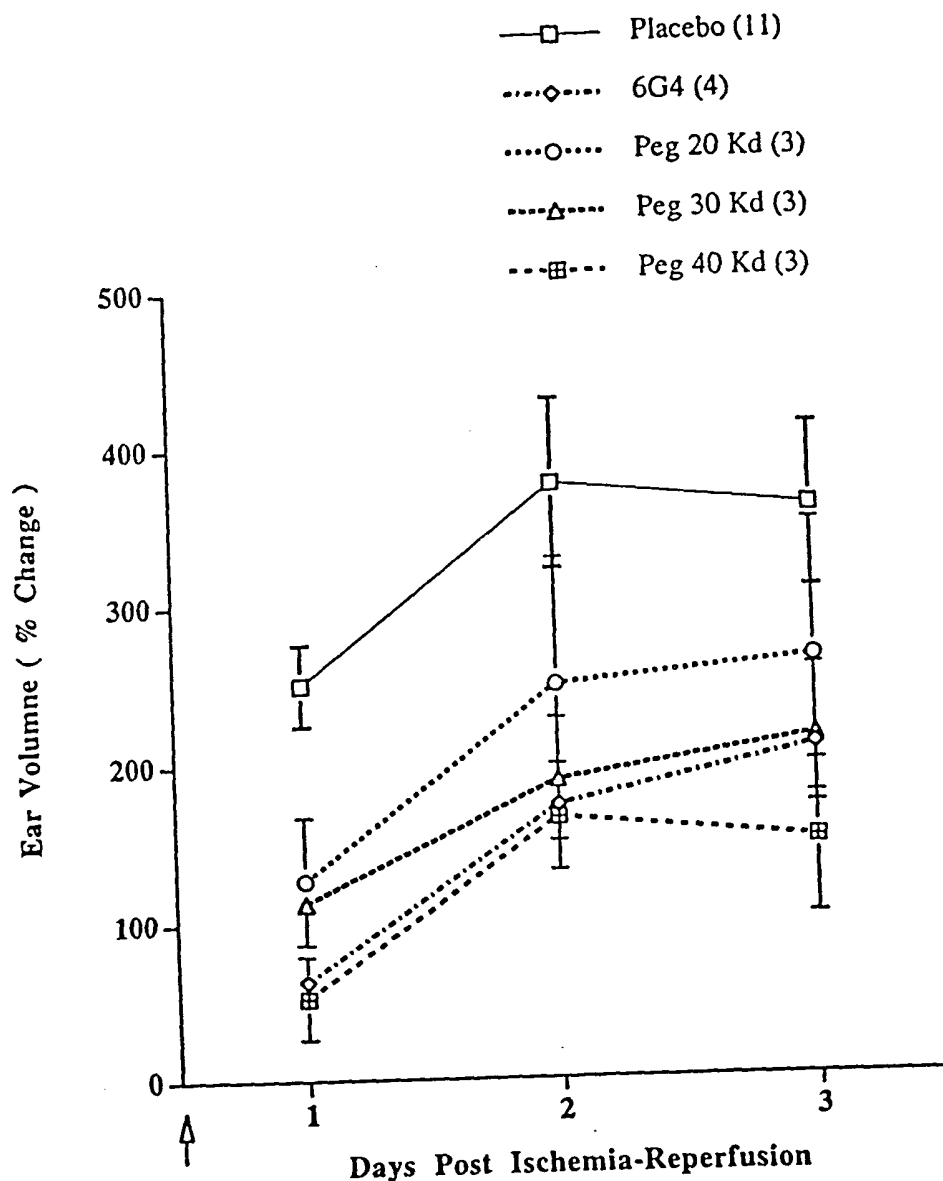


FIG. 70E

The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations :
 Single Dose (5 mg/kg)
 administered IV at time
 of reperfusion

FIG. 71